

*Jan Delaval please*

Access DB# 110639

## SEARCH REQUEST FORM

### Scientific and Technical Information Center

Requester's Full Name: Sabika Qazi Examiner #: 74141 Date: 12/16/03

Art Unit: 166 Phone Number 305-3910 Serial Number: 01/939208

Mail Box and Bldg/Room Location: 2D19 Results Format Preferred (circle):  PAPER  DISK  E-MAIL

If more than one search is submitted, please prioritize searches in order of need.

Please provide a detailed statement of the search topic, and describe as specifically as possible the subject matter to be searched.

Include the elected species or structures, keywords, synonyms, acronyms, and registry numbers, and combine with the concept or utility of the invention. Define any terms that may have a special meaning. Give examples or relevant citations, authors, etc, if known. Please attach a copy of the cover sheet, pertinent claims, and abstract.

Title of Invention: Angiogenesis agent

*See 07/779,331*

Inventors (please provide full names): Gregory E. Agoston et al

Earliest Priority Filing Date: 2/8/2001

\*For Sequence Searches Only\* Please include all pertinent information (parent, child, divisional, or issued patent numbers) along with the appropriate serial number.

Please search for elected species of  
Cl. 3, (Structures attached) and compounds  
of formula in cl 1

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***** STAFF USE ONLY		Type of Search	Vendors and cost where applicable
Searcher:	<u>Jan</u>	NA Sequence (#)	STN <input checked="" type="checkbox"/>
Searcher Phone #:	<u>4498</u>	AA Sequence (#)	Dialog <input checked="" type="checkbox"/>
Searcher Location:		Structure (#)	Questel/Orbit <input checked="" type="checkbox"/>
Date Searcher Picked Up:	<u>12/17/03</u>	Bibliographic	Dr.Link <input checked="" type="checkbox"/>
Date Completed:	<u>12/17/03</u>	Litigation	Lexis/Nexis <input checked="" type="checkbox"/>
Searcher Prep & Review Time:		Fulltext	Sequence Systems <input checked="" type="checkbox"/>
Clerical Prep Time:	<u>20</u>	Patent Family	WWW/Internet <input checked="" type="checkbox"/>
Online Time:	<u>+75</u>	Other	Other (specify) _____

Sabika:  
Claim 1b, page 2, contains (an) error:



Also, I had to leave  $R_a$ ,  $R_h$ ,  $R_{hz}$ ,  
 $R_g$ ,  $R_S$ , and  $R_{gz}$  open, as they are  
"optionally" substituted ...!

Broaded,  
from applicants'  
own references

Selected  
Species

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=> fil reg  
FILE 'REGISTRY' ENTERED AT 09:14:10 ON 21 DEC 2003  
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.  
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Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 19 DEC 2003 HIGHEST RN 628722-21-4  
DICTIONARY FILE UPDATES: 19 DEC 2003 HIGHEST RN 628722-21-4

TSCA INFORMATION NOW CURRENT THROUGH JULY 14, 2003

Please note that search-term pricing does apply when conducting SmartSELECT searches.

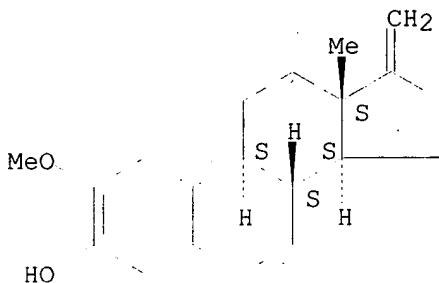
Crossover limits have been increased. See HELP CROSSOVER for details.

Experimental and calculated property data are now available. For more information enter HELP PROP at an arrow prompt in the file or refer to the file summary sheet on the web at:  
<http://www.cas.org/ONLINE/DBSS/registryss.html>

=> d 13 ide can

L3 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2003 ACS on STN  
RN 431901-73-4 REGISTRY  
CN Estra-1,3,5(10)-trien-3-ol, 2-methoxy-17-methylene- (9CI) (CA  
INDEX NAME)  
FS STEREOSEARCH  
MF C20 H26 O2  
SR CA  
LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL

Absolute stereochemistry.



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

2 REFERENCES IN FILE CA (1907 TO DATE)  
2 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 137:47357

REFERENCE 2: 137:6309

=> fil uspatall  
FILE 'USPATFULL' ENTERED AT 09:14:17 ON 21 DEC 2003  
CA INDEXING COPYRIGHT (C) 2003 AMERICAN CHEMICAL SOCIETY (ACS)

FILE 'USPAT2' ENTERED AT 09:14:17 ON 21 DEC 2003  
 CA INDEXING COPYRIGHT (C) 2003 AMERICAN CHEMICAL SOCIETY (ACS)

=> d bib abs hitstr 16

L6 ANSWER 1 OF 1 USPATFULL on STN  
 AN 2002:157823 USPATFULL  
 TI Antiangiogenic agents  
 IN Agoston, Gregory E., Germantown, MD, UNITED STATES  
     Shah, Jamshed H., Brookeville, MD, UNITED STATES  
     Hunsucker, Kimberly A., Germantown, MD, UNITED STATES  
     Pribluda, Victor S., Silver Spring, MD, UNITED STATES  
     LaVallee, Theresa M., Rockville, MD, UNITED STATES  
     Green, Shawn J., Vienna, VA, UNITED STATES  
     Herbstreit, Christopher J., Rockville, VA, UNITED STATES  
     Zhan, Xiaoguo H., Montgomery Village, MD, UNITED STATES  
     Treston, Anthony M., Rockville, MD, UNITED STATES  
 PI US 2002082433 A1 20020627  
 AI US 2001-939208 A1 20010824 (9)  
 RLI Continuation-in-part of Ser. No. US 2001-933894, filed on 21 Aug 2001,  
     PENDING Continuation-in-part of Ser. No. US 2000-641327, filed on 18 Aug  
     2000, PENDING  
 PRAI US 2000-253385P 20001127 (60)  
     US 2000-255302P 20001213 (60)  
     US 2001-278250P 20010323 (60)  
 DT Utility  
 FS APPLICATION  
 LREP John S. Pratt, KILPATRICK STOCKTON LLP, Suite 2800, 1100 Peachtree  
     Street, Atlanta, GA, 30309-4530  
 CLMN Number of Claims: 92  
 ECL Exemplary Claim: 1  
 DRWN No Drawings  
 LN.CNT 2637

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

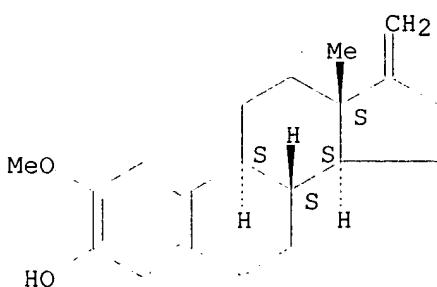
AB Compositions and methods for treating mammalian disease characterized by  
     undesirable angiogenesis by administering derivatives of  
     2-methoxyestradiol of the general formula: ##STR1##

wherein the variables are defined in the specification.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT 431901-73-4P  
     (preparation of 2-methoxyestradiol derivs. as antiangiogenic agents)  
 RN 431901-73-4 USPATFULL  
 CN Estra-1,3,5(10)-trien-3-ol, 2-methoxy-17-methylene- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



=> fil hcaplus  
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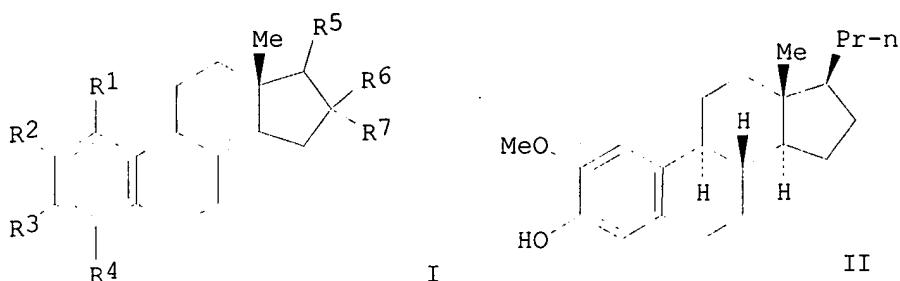
FILE COVERS 1907 - 21 Dec 2003 VOL 139 ISS 26  
FILE LAST UPDATED: 19 Dec 2003 (20031219/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

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L7 ANSWER 1 OF 2 HCAPLUS COPYRIGHT 2003 ACS on STN  
AN 2002:488275 HCAPLUS  
DN 137:47357  
ED Entered STN: 28 Jun 2002  
TI Preparation of 2-methoxyestradiol derivatives as antiangiogenic agents  
IN Agoston, Gregory E.; Shah, Jamshed H.; Hunsucker, Kimberly A.; Pribluda,  
Victor S.; Lavallee, Theresa M.; Green, Shawn J.; Herbstritt, Christopher  
J.; Zhan, Xiaoguo H.; Treston, Anthony M.  
PA USA  
SO U.S. Pat. Appl. Publ., 37 pp., Cont.-in-part of U. S. Ser. No. 933,894.  
CODEN: USXXCO  
DT Patent  
LA English  
IC ICM C07J041-00  
ICS C07J043-00; C07J001-00; A61K031-704; A61K031-58; A61K031-56;  
C07C247-00; A61K031-655; C07J009-00  
NCL 552544000  
CC 32-3 (Steroids)  
Section cross-reference(s): 1  
FAN.CNT 2

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI US 2002082433	A1	20020627	US 2001-939208	20010824
PRAI US 2000-641327	A2	20000818		
US 2000-253385P	P	20001127		
US 2000-255302P	P	20001213		
US 2001-278250P	P	20010323		
US 2001-933894	A2	20010821		
OS MARPAT 137:47357				
GI				



AB 2-Methoxyestradiol derivs. of formula I [R<sub>1</sub>, R<sub>4</sub> = H, halo, CN, OH, NH<sub>2</sub>, etc.; R<sub>2</sub> = N<sub>3</sub>, CN, OMe, alkenyl, alkynyl, alkoxy, NH<sub>2</sub>, etc.; R<sub>3</sub> = OH, OAc; R<sub>5</sub> = alkyl, alkenyl, (di)alkylamino, OH, alkylene, etc.; R<sub>6</sub>, R<sub>7</sub> = H, alkyl, alkenyl, alkynyl, halo, etc.] are prepared for treating mammalian disease characterized by undesirable angiogenesis. Thus, II was prepared from 2-methoxyestradiol and propyltriphenylphosphonium bromide. The IC<sub>50</sub> of II against MDA-MB-231 breast tumor cells was 51.31  $\mu$ M.

ST methoxyestradiol deriv prep antiangiogenic; estradiol deriv prep antiangiogenic; antitumor methoxyestradiol deriv prep; antimitotic methoxyestradiol deriv prep

IT Structure-activity relationship  
(antitumor; preparation of 2-methoxyestradiol derivs. as antiangiogenic agents)

IT Mitosis  
(inhibitors; preparation of 2-methoxyestradiol derivs. as antiangiogenic agents)

IT Angiogenesis inhibitors

Antitumor agents

Human

Mammary gland, neoplasm

Neoplasm

(preparation of 2-methoxyestradiol derivs. as antiangiogenic agents)

IT 362-07-2, 2-Methoxyestradiol

RL: PAC (Pharmacological activity); RCT (Reactant); BIOL (Biological study); RACT (Reactant or reagent)

(preparation of 2-methoxyestradiol derivs. as antiangiogenic agents)

IT 53-63-4P, Estra-1,3,5(10)-trien-3-ol 6301-87-7P 431901-72-3P

431901-73-4P 431901-75-6P 431901-77-8P 431901-91-6P

RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

(preparation of 2-methoxyestradiol derivs. as antiangiogenic agents)

IT 1818-12-8P 4953-96-2P 6298-51-7P 6599-97-9P 7291-57-8P

10332-20-4P 32162-96-2P 41259-43-2P 94440-60-5P 165619-07-8P

165881-61-8P 229486-18-4P 431901-68-7P 431901-69-8P 431901-70-1P

431901-71-2P 431901-74-5P 431901-78-9P 431901-87-0P 431901-90-5P

431901-92-7P 431901-93-8P 431901-94-9P 431901-95-0P 431901-96-1P

431901-97-2P 431901-98-3P 431901-99-4P 431902-00-0P 431902-01-1P

431902-02-2P 431902-03-3P 431902-04-4P 431902-05-5P 431902-06-6P

431902-07-7P 431902-08-8P 431902-09-9P 438044-29-2P 438044-30-5P

438044-35-0P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of 2-methoxyestradiol derivs. as antiangiogenic agents)

IT 53-16-7, Estrone, reactions 106-95-6, Allyl bromide, reactions

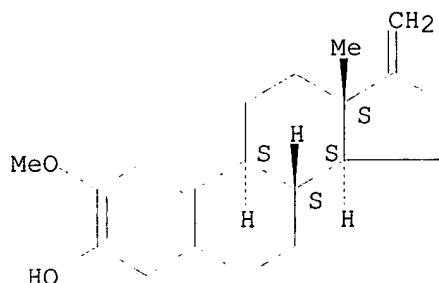
1779-51-7, Butyltriphenylphosphonium bromide 4784-77-4, Crotyl bromide

5815-08-7 6228-47-3, Propyltriphenylphosphonium bromide

RL: RCT (Reactant); RACT (Reactant or reagent)

(preparation of 2-methoxyestradiol derivs. as antiangiogenic agents)  
IT 26356-54-7P 26357-07-3P 93949-26-9P 431901-79-0P 431901-81-4P  
431901-82-5P 431901-83-6P 431901-84-7P 431901-85-8P 431901-89-2P  
438044-31-6P 438044-32-7P 438044-33-8P  
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
(preparation of 2-methoxyestradiol derivs. as antiangiogenic agents)  
IT 431901-73-4P  
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)  
(preparation of 2-methoxyestradiol derivs. as antiangiogenic agents)  
RN 431901-73-4 HCAPLUS  
CN Estra-1,3,5(10)-trien-3-ol, 2-methoxy-17-methylene- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L7 ANSWER 2 OF 2 HCAPLUS COPYRIGHT 2003 ACS on STN  
AN 2002:408687 HCAPLUS  
DN 137:6309  
ED Entered STN: 31 May 2002  
TI Preparation of 2-methoxyestradiol analogs as antiangiogenic agents  
IN Agoston, Gregory; Shah, Jamshed H.; Hunsucker, Kimberly A.; Pribluda, Victor; Lavallee, Theresa M.; Green, Shawn J.; Herbstritt, Christopher J.; Zhan, Xiaoguo H.; Treston, Anthony  
PA Entremed, Inc., USA  
SO PCT Int. Appl., 86 pp.  
CODEN: PIXXD2

DT Patent  
LA English  
IC ICM C07J001-00  
CC 32-3 (Steroids)

Section cross-reference(s): 1, 2, 63

FAN.CNT 2

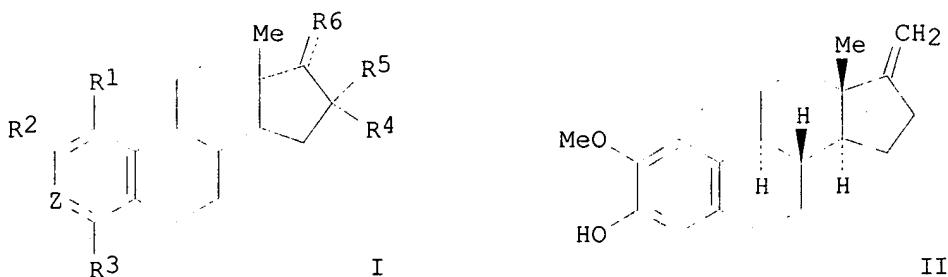
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PI	WO 2002042319	A2	20020530	WO 2001-US26490	20010824
	WO 2002042319	A3	20030313		
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	RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
	AU 2001088386	A5	20020603	AU 2001-88386	20010824
	EP 1343803	A2	20030917	EP 2001-968112	20010824
	R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,			

IE, SI, LT, LV, FI, RO, MK, CY, AL, TR

PRAI US 2000-253385P P 20001127  
 US 2000-255302P P 20001213  
 US 2001-278250P P 20010323  
 US 2001-933894 A 20010821  
 WO 2001-US26490 W 20010824

OS MARPAT 137:6309

GI



AB 2-Methoxyestradiol analogs, such as I [R1, R3 = H, halo, CN, alkyl, OH, CH<sub>2</sub>OH, NH<sub>2</sub>, alkylamino; R2 = N3, CN, C.tplbond.CR, C=CHR, C.tplbond.CH, OR, amino; R = H, alkyl; Z = COH, COAc; dashed bond = single bond or double bond; R6 = H, OH, O, oxime, amino, alkyl, alkenyl; R4, R5 = H, alkyl, alkenyl, alkynyl], were prepared for treating mammalian disease characterized by undesirable angiogenesis. Thus, 2-methoxyestradiol analog II was prepared by the reaction of methyltriphenylphosphonium bromide and 2-methoxyestrone. In vitro evaluation against MDA-MB-231 breast tumor cells and HUVEC endothelial cells, II showed IC<sub>50</sub> 0.24±0 and 0.19±0.19 resp.

ST methoxyestradiol deriv prepn antiangiogenic antitumor; estradiol methoxy deriv prepn antiangiogenic antitumor

IT Cell proliferation  
 (inhibition; preparation of 2-methoxyestradiol derivs. as antiangiogenic agents)

IT Mammary gland, neoplasm  
 (inhibitors; preparation of 2-methoxyestradiol derivs. as antiangiogenic agents)

IT Antitumor agents  
 (mammary gland; preparation of 2-methoxyestradiol derivs. as antiangiogenic agents)

IT Angiogenesis inhibitors  
 Human  
 (preparation of 2-methoxyestradiol derivs. as antiangiogenic agents)

IT Estrogens  
 RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)  
 (preparation of 2-methoxyestradiol derivs. as antiangiogenic agents)

IT 53-63-4P, Estra-1,3,5(10)-trien-3-ol 431901-72-3P 431901-73-4P  
 431901-75-6P 431901-77-8P 431901-83-6P 431901-89-2P 431901-91-6P  
 RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

(preparation of 2-methoxyestradiol derivs. as antiangiogenic agents)

IT 1818-12-8P 4953-96-2P 6298-51-7P 6301-87-7P 6599-97-9P  
 7291-57-8P 10332-20-4P 32162-96-2P 41259-43-2P 94440-60-5P  
 165619-07-8P 165881-61-8P 192062-02-5P 229486-18-4P 431901-68-7P

431901-69-8P 431901-70-1P 431901-71-2P 431901-74-5P 431901-76-7P  
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RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of 2-methoxyestradiol derivs. as antiangiogenic agents)

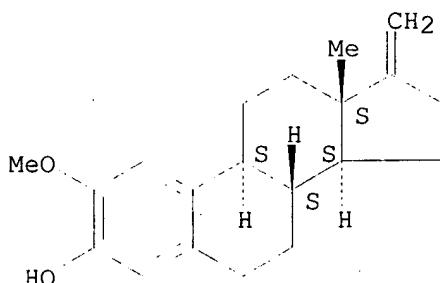
IT 53-16-7, Estrone, reactions 64-18-6, Formic acid, reactions 100-39-0,  
 Benzyl bromide 106-95-6, Allyl bromide, reactions 362-07-2,  
 2-Methoxyestradiol 1530-32-1, Ethyl triphenylphosphonium bromide  
 1779-49-3, Methyl triphenylphosphonium bromide 1779-51-7, Butyl  
 triphenylphosphonium bromide 4784-77-4, Crotyl bromide 5815-08-7,  
 tert-Butoxy bis(dimethylamino)methane 6228-47-3, Propyl  
 triphenylphosphonium bromide 17640-15-2, Methyl cyanoformate  
 RL: RCT (Reactant); RACT (Reactant or reagent)

IT 26356-54-7P 26357-07-3P 93949-26-9P 431901-79-0P 431901-80-3P  
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 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT  
 (Reactant or reagent)

IT 431901-73-4P  
 RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic  
 preparation); THU (Therapeutic use); BIOL (Biological study); PREP  
 (Preparation); RACT (Reactant or reagent); USES (Uses)

RN 431901-73-4 HCAPLUS  
 CN Estra-1,3,5(10)-trien-3-ol, 2-methoxy-17-methylene- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



=> => fil reg

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STRUCTURE FILE UPDATES: 19 DEC 2003 HIGHEST RN 628722-21-4  
 DICTIONARY FILE UPDATES: 19 DEC 2003 HIGHEST RN 628722-21-4

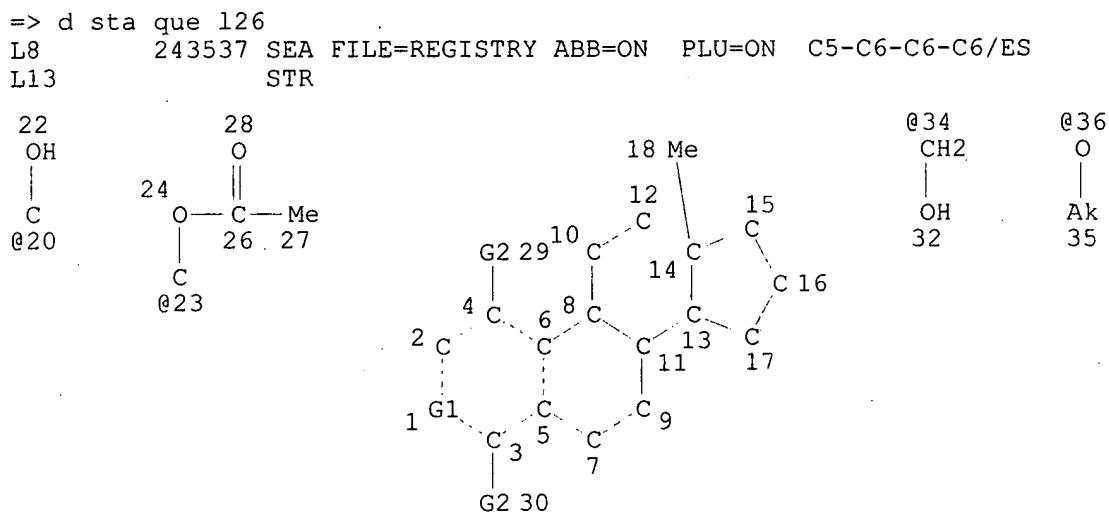
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Experimental and calculated property data are now available. For more information enter HELP PROP at an arrow prompt in the file or refer to the file summary sheet on the web at:  
<http://www.cas.org/ONLINE/DBSS/registryss.html>



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VAR G2=H/X/CN/AK/OH/34/NH2/36/38/39

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CONNECT IS M1 RC AT 16  
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DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:

RSPEC 1  
NUMBER OF NODES IS 36

STEREO ATTRIBUTES: NONE

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L24 STR

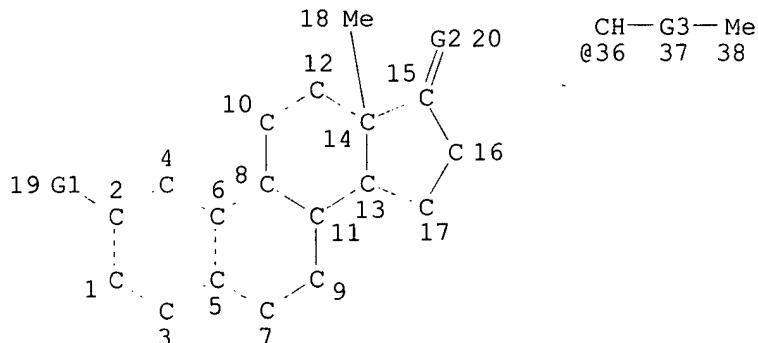
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$\text{CH}=\text{CH}-\text{Me}$   
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$\text{CH}_2-\text{OH}$   
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$\text{N}\sim\text{CHO}$   
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$\text{N}\sim\text{O}$   
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VAR G2=34/36/CH2

REP G3=(0-1) CH2

NODE ATTRIBUTES:

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GRAPH ATTRIBUTES:

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L26 10 SEA FILE=REGISTRY SUB=L15 CSS FUL L24

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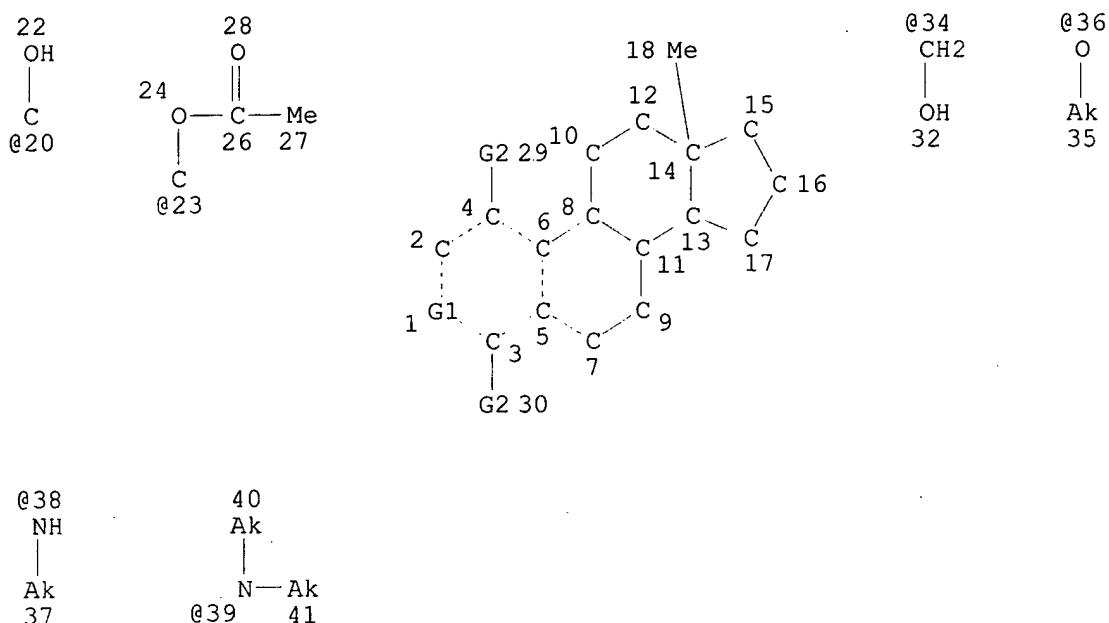
10 ANSWERS

SEARCH TIME: 00.00.01

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L8 243537 SEA FILE=REGISTRY ABB=ON PLU=ON C5-C6-C6-C6/ES

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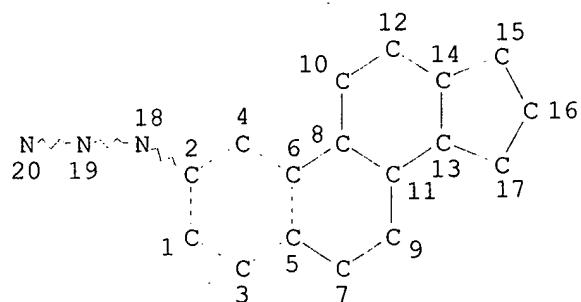
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 DEFAULT MLEVEL IS ATOM  
 DEFAULT ECLEVEL IS LIMITED

## GRAPH ATTRIBUTES:

RSPEC 1  
 NUMBER OF NODES IS 36

## STEREO ATTRIBUTES: NONE

L15 4643 SEA FILE=REGISTRY SUB=L8 CSS FUL L13  
 L30 STR



claim 91

## NODE ATTRIBUTES:

CONNECT IS M1 RC AT 1  
 CONNECT IS M1 RC AT 3  
 CONNECT IS M1 RC AT 4  
 CONNECT IS M1 RC AT 15  
 CONNECT IS M1 RC AT 16  
 DEFAULT MLEVEL IS ATOM  
 DEFAULT ECLEVEL IS LIMITED

## GRAPH ATTRIBUTES:

RSPEC 1

NUMBER OF NODES IS 20

## STEREO ATTRIBUTES: NONE

L32 0 SEA FILE=REGISTRY SUB=L15 CSS FUL L30

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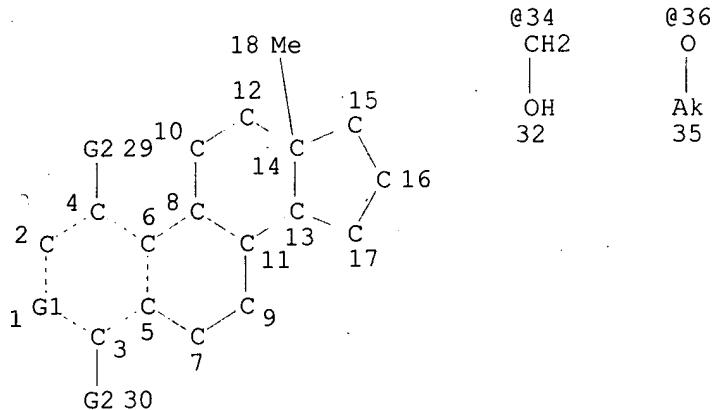
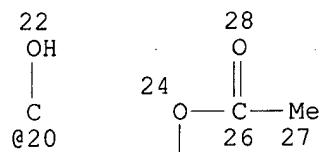
SEARCH TIME: 00.00.01

0 ANSWERS

=&gt; d sta que 135

L8 243537 SEA FILE=REGISTRY ABB=ON PLU=ON C5-C6-C6-C6/ES

L13 STR



@38

40

NH  
Ak  
37Ak  
N—Ak  
39 41

VAR G1=20/23

VAR G2=H/X/CN/AK/OH/34/NH2/36/38/39

## NODE ATTRIBUTES:

CONNECT IS M1 RC AT 2

CONNECT IS M1 RC AT 15

CONNECT IS M1 RC AT 16

DEFAULT MLEVEL IS ATOM

DEFAULT ECLEVEL IS LIMITED

## GRAPH ATTRIBUTES:

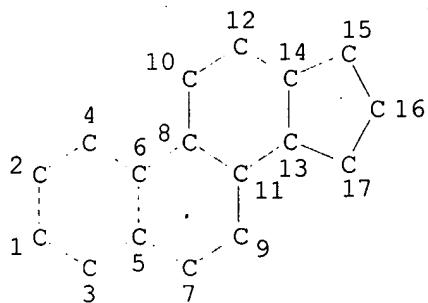
RSPEC 1

NUMBER OF NODES IS 36

## STEREO ATTRIBUTES: NONE

L15 4643 SEA FILE=REGISTRY SUB=L8 CSS FUL L13

L33 STR



## NODE ATTRIBUTES:

CONNECT IS M1 RC AT 1  
 CONNECT IS M1 RC AT 3  
 CONNECT IS M1 RC AT 4  
 CONNECT IS M1 RC AT 16  
 DEFAULT MLEVEL IS ATOM  
 DEFAULT ECLEVEL IS LIMITED

## GRAPH ATTRIBUTES:

RSPEC 2  
 NUMBER OF NODES IS 17

## STEREO ATTRIBUTES: NONE

L35 0 SEA FILE=REGISTRY SUB=L15 CSS FUL L33

100.0% PROCESSED 4643 ITERATIONS  
 SEARCH TIME: 00.00.01

0 ANSWERS

=> d his 126-

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 L27 9 S L26 NOT L3  
 L28 STR  
 L29 0 S L28 CSS SAM SUB=L15  
 L30 STR L28  
 L31 0 S L30 CSS SAM SUB=L15  
 L32 0 S L30 CSS FUL SUB=L15  
     SAV L32 QAZI939E/A  
 L33 STR L30  
 L34 0 S L33 CSS SAM SUB=L15  
 L35 0 S L33 CSS FULL SUB=L15  
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FILE 'HCAOLD' ENTERED AT 09:46:24 ON 21 DEC 2003  
 L36 0 S L27

FILE 'USPATFULL, USPAT2' ENTERED AT 09:46:29 ON 21 DEC 2003  
 L37 5 S L27

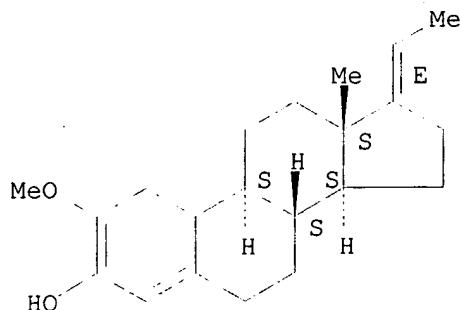
FILE 'HCAPLUS' ENTERED AT 09:46:41 ON 21 DEC 2003  
 L38 9 S L27  
 L39 2 S L38 AND ENTREMED?/PA,CS  
 L40 3 S L38 AND (AGOSTON ? OR SHAH ? OR HUNSUCKER ? OR PRIBLUDA ? OR  
 L41 9 S L38-L40

FILE 'REGISTRY' ENTERED AT 09:48:58 ON 21 DEC 2003

=> d ide can tot 127

L27 ANSWER 1 OF 9 REGISTRY COPYRIGHT 2003 ACS on STN  
 RN 594873-87-7 REGISTRY  
 CN 19-Norpregna-1,3,5(10),17(20)-tetraen-3-ol, 2-methoxy-, (17E)- (9CI) (CA INDEX NAME)  
 FS STEREOSEARCH  
 MF C21 H28 O2  
 SR CA  
 LC STN Files: CA, CAPLUS

Absolute stereochemistry.  
 Double bond geometry as shown.



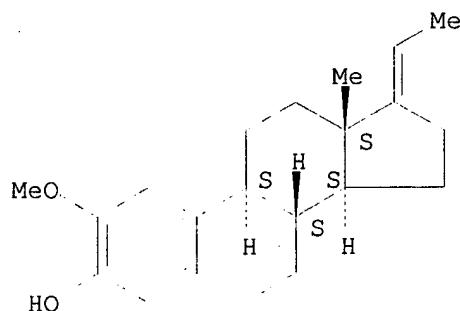
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1 REFERENCES IN FILE CA (1907 TO DATE)  
 1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 139:224972

L27 ANSWER 2 OF 9 REGISTRY COPYRIGHT 2003 ACS on STN  
 RN 431901-75-6 REGISTRY  
 CN 19-Norpregna-1,3,5(10),17(20)-tetraen-3-ol, 2-methoxy- (9CI) (CA INDEX NAME)  
 FS STEREOSEARCH  
 MF C21 H28 O2  
 SR CA  
 LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL

Absolute stereochemistry.  
 Double bond geometry unknown.



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

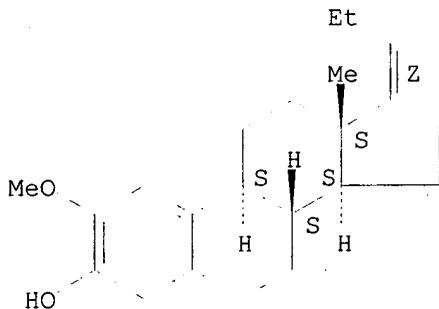
2 REFERENCES IN FILE CA (1907 TO DATE)  
 2 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 137:47357

REFERENCE 2: 137:6309

L27 ANSWER 3 OF 9 REGISTRY COPYRIGHT 2003 ACS on STN  
 RN 431901-72-3 REGISTRY  
 CN Estra-1,3,5(10)-trien-3-ol, 2-methoxy-17-propylidene-, (17Z)- (9CI) (CA INDEX NAME)  
 FS STEREOSEARCH  
 MF C22 H30 O2  
 SR CA  
 LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL

Absolute stereochemistry.  
 Double bond geometry as shown.



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

3 REFERENCES IN FILE CA (1907 TO DATE)  
 3 REFERENCES IN FILE CAPLUS (1907 TO DATE)

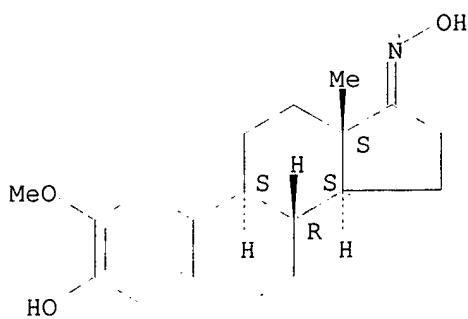
REFERENCE 1: 139:224972

REFERENCE 2: 137:47357

REFERENCE 3: 137:6309

L27 ANSWER 4 OF 9 REGISTRY COPYRIGHT 2003 ACS on STN  
 RN 431901-69-8 REGISTRY  
 CN Estra-1,3,5(10)-trien-17-one, 3-hydroxy-2-methoxy-, oxime (9CI) (CA INDEX NAME)  
 FS STEREOSEARCH  
 MF C19 H25 N O3  
 SR CA  
 LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL

Absolute stereochemistry.  
 Double bond geometry unknown.



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

3 REFERENCES IN FILE CA (1907 TO DATE)  
3 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 139:224972

REFERENCE 2: 137:47357

REFERENCE 3: 137:6309

L27 ANSWER 5 OF 9 REGISTRY COPYRIGHT 2003 ACS on STN

RN 229486-17-3 REGISTRY

CN 19-Norpregna-1,3,5(10),17(20)-tetraen-3-ol, 2-methoxy-, (17Z)- (9CI) (CA INDEX NAME)

FS STEREOSEARCH

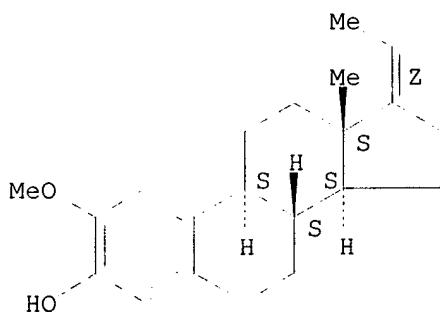
MF C21 H28 O2

SR CA

LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL

Absolute stereochemistry.

Double bond geometry as shown.



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

4 REFERENCES IN FILE CA (1907 TO DATE)  
4 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 137:370278

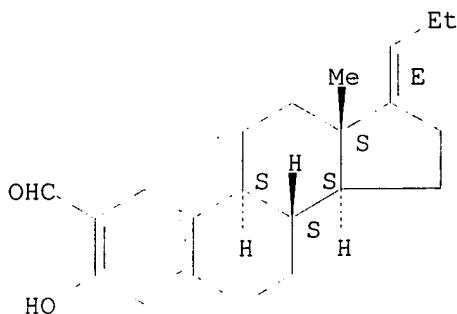
REFERENCE 2: 135:358085

REFERENCE 3: 133:350395

REFERENCE 4: 131:88083

L27 ANSWER 6 OF 9 REGISTRY COPYRIGHT 2003 ACS on STN  
 RN 208758-47-8 REGISTRY  
 CN Estra-1,3,5(10)-triene-2-carboxaldehyde, 3-hydroxy-17-propylidene-, (17E)-  
 (9CI) (CA INDEX NAME)  
 FS STEREOSEARCH  
 MF C22 H28 O2  
 SR CA  
 LC STN Files: CA, CAPLUS, CASREACT, TOXCENTER, USPATFULL

Absolute stereochemistry.  
 Double bond geometry as shown.



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

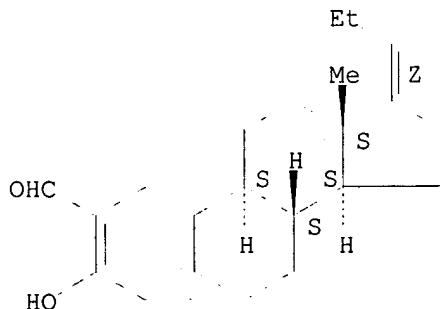
2 REFERENCES IN FILE CA (1907 TO DATE)  
 2 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 138:348841

REFERENCE 2: 129:54482

L27 ANSWER 7 OF 9 REGISTRY COPYRIGHT 2003 ACS on STN  
 RN 208758-28-5 REGISTRY  
 CN Estra-1,3,5(10)-triene-2-carboxaldehyde, 3-hydroxy-17-propylidene-, (17Z)-  
 (9CI) (CA INDEX NAME)  
 FS STEREOSEARCH  
 MF C22 H28 O2  
 SR CA  
 LC STN Files: CA, CAPLUS, CASREACT, TOXCENTER, USPATFULL

Absolute stereochemistry.  
 Double bond geometry as shown.



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

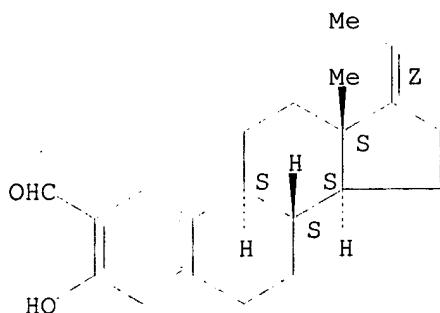
2 REFERENCES IN FILE CA (1907 TO DATE)  
 2 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 138:348841

REFERENCE 2: 129:54482

L27 ANSWER 8 OF 9 REGISTRY COPYRIGHT 2003 ACS on STN  
 RN 208758-27-4 REGISTRY  
 CN 19-Norpregna-1,3,5(10),17(20)-tetraene-2-carboxaldehyde, 3-hydroxy-,  
 (17Z)- (9CI) (CA INDEX NAME)  
 FS STEREOSEARCH  
 MF C21 H26 O2  
 SR CA  
 LC STN Files: CA, CAPLUS, CASREACT, TOXCENTER, USPATFULL

Absolute stereochemistry.  
 Double bond geometry as shown.



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

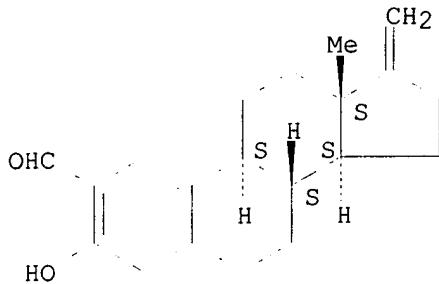
2 REFERENCES IN FILE CA (1907 TO DATE)  
 2 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 138:348841

REFERENCE 2: 129:54482

L27 ANSWER 9 OF 9 REGISTRY COPYRIGHT 2003 ACS on STN  
 RN 208758-26-3 REGISTRY  
 CN Estra-1,3,5(10)-triene-2-carboxaldehyde, 3-hydroxy-17-methylene- (9CI)  
 (CA INDEX NAME)  
 FS STEREOSEARCH  
 MF C20 H24 O2  
 SR CA  
 LC STN Files: CA, CAPLUS, CASREACT, TOXCENTER, USPATFULL

Absolute stereochemistry.



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

2 REFERENCES IN FILE CA (1907 TO DATE)  
2 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 138:348841

REFERENCE 2: 129:54482

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CA INDEXING COPYRIGHT (C) 2003 AMERICAN CHEMICAL SOCIETY (ACS)

FILE 'USPAT2' ENTERED AT 09:49:31 ON 21 DEC 2003  
CA INDEXING COPYRIGHT (C) 2003 AMERICAN CHEMICAL SOCIETY (ACS)

=> d 137 bib abs hitstr tot

L37 ANSWER 1 OF 5 USPATFULL on STN  
AN 2003:226354 USPATFULL  
TI 2-substituted prega-1,3,5(10) triene and chola-1,3,5(10) triene derivatives and their biological activity  
IN Hesse, Robert Henry, Winchester, MA, UNITED STATES  
Setty, Sundara Katugam Srinivasasetty, Cambridge, MA, UNITED STATES  
Pechet, Maurice Murdoch, Cambridge, MA, UNITED STATES  
Gile, Michael, Methuen, MA, UNITED STATES  
PI US 2003158167 A1 20030821  
AI US 2003-275257 A1 20030313 (10)  
WO 2001-GB2103 20010511  
DT Utility  
FS APPLICATION  
LREP BACON & THOMAS, PLLC, 625 SLATERS LANE, FOURTH FLOOR, ALEXANDRIA, VA, 22314  
CLMN Number of Claims: 13  
ECL Exemplary Claim: 1  
DRWN No Drawings  
LN.CNT 978

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Compounds of formula (I) in which: R.<sup>1</sup> represents a hydrogen atom or an O-protecting group; R.<sup>2</sup> represents a hydroxyl, lower alkoxy, carboxaldehyde, lower alk-1-enyl or hydroxy- or lower alkoxy-substituted lower alkyl group; R.<sup>3</sup> represents a methyl group having α- or β-configuration; X represents a C.<sub>1-3</sub> alkylene group or a valence bond; Y represents a carboxaldehyde group or a group of formula --C(R.<sup>4</sup>)(R.<sup>5</sup>)OR.<sup>1</sup> where R.<sup>1</sup> is as defined above and R.<sup>4</sup> and R.<sup>5</sup>, which may be the same or different, are each selected from hydrogen atoms, alkyl, alkenyl and alkynyl groups such that the total carbon content of R.<sup>4</sup> and R.<sup>5</sup> does not exceed

three atoms, with the proviso that X is a valence bond when both R.<sup>4</sup> and R.<sup>5</sup> are other than hydrogen; and the dotted line signifies that a double bond may optionally be present at the 16(17)-position exhibit potent cell modulating activity, including antiproliferative and antiangiogenic effects.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT 229486-17-3P

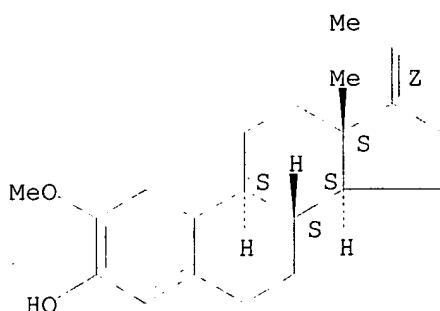
(preparation of 2-substituted pregnatriene and cholatriene derivs. with antiproliferative and antiangiogenic activity)

RN 229486-17-3 USPATFULL

CN 19-Norpregna-1,3,5(10),17(20)-tetraen-3-ol, 2-methoxy-, (17Z)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.



L37 ANSWER 2 OF 5 USPATFULL on STN

AN 2002:157823 USPATFULL

TI Antiangiogenic agents

IN Agoston, Gregory E., Germantown, MD, UNITED STATES

Shah, Jamshed H., Brookeville, MD, UNITED STATES

Hunsucker, Kimberly A., Germantown, MD, UNITED STATES

Pribluda, Victor S., Silver Spring, MD, UNITED STATES

LaVallee, Theresa M., Rockville, MD, UNITED STATES

Green, Shawn J., Vienna, VA, UNITED STATES

Herbstreit, Christopher J., Rockville, VA, UNITED STATES

Zhan, Xiaoguo H., Montgomery Village, MD, UNITED STATES

Treston, Anthony M., Rockville, MD, UNITED STATES

PI US 2002082433 A1 20020627

AI US 2001-939208 A1 20010824 (9)

RLI Continuation-in-part of Ser. No. US 2001-933894, filed on 21 Aug 2001,  
PENDING Continuation-in-part of Ser. No. US 2000-641327, filed on 18 Aug  
2000, PENDING

PRAI US 2000-253385P 20001127 (60)

US 2000-255302P 20001213 (60)

US 2001-278250P 20010323 (60)

DT Utility

FS APPLICATION

LREP John S. Pratt, KILPATRICK STOCKTON LLP, Suite 2800, 1100 Peachtree  
Street, Atlanta, GA, 30309-4530

CLMN Number of Claims: 92

ECL Exemplary Claim: 1

DRWN No Drawings

LN.CNT 2637

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Compositions and methods for treating mammalian disease characterized by undesirable angiogenesis by administering derivatives of  
2-methoxyestradiol of the general formula: ##STR1##

wherein the variables are defined in the specification.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT 431901-72-3P 431901-75-6P

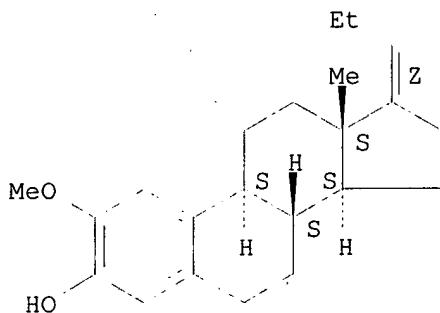
(preparation of 2-methoxyestradiol derivs. as antiangiogenic agents)

RN 431901-72-3 USPATFULL

CN Estra-1,3,5(10)-trien-3-ol, 2-methoxy-17-propylidene-, (17Z)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.

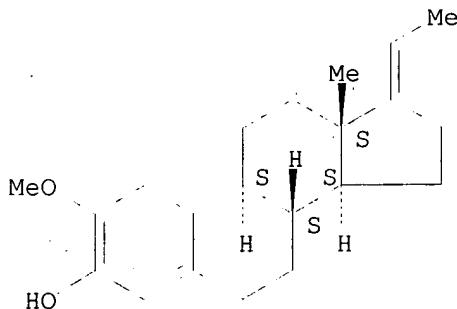


RN 431901-75-6 USPATFULL

CN 19-Norpregna-1,3,5(10),17(20)-tetraen-3-ol, 2-methoxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry unknown.



IT 431901-69-8P

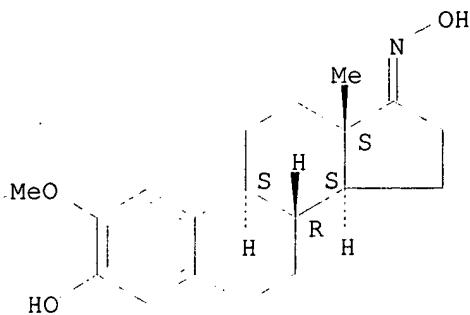
(preparation of 2-methoxyestradiol derivs. as antiangiogenic agents)

RN 431901-69-8 USPATFULL

CN Estra-1,3,5(10)-trien-17-one, 3-hydroxy-2-methoxy-, oxime (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry unknown.



L37 ANSWER 3 OF 5 USPATFULL on STN

AN 2000:41031 USPATFULL

TI Estrone sulfamate inhibitors of estrone sulfatase, and associated pharmaceutical compositions and methods of use

IN Tanabe, Masato, Palo Alto, CA, United States  
Peters, Richard H., San Jose, CA, United States  
Chao, Wan-Ru, Sunnyvale, CA, United States  
Shigeno, Kazuhiko, Saitama, CA, United States

PA SRI International, Menlo Park, CA, United States (U.S. corporation)

PI US 6046186 20000404

AI US 1997-997416 19971224 (8)

DT Utility

FS Granted

EXNAM Primary Examiner: Raymond, Richard L.; Assistant Examiner: Coleman, Brenda

LREP Reed, Dianne E. Reed & Associates

CLMN Number of Claims: 65

ECL Exemplary Claim: 1

DRWN No Drawings

LN.CNT 3007

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Novel compounds useful as inhibitors of estrone sulfatase are provided. The compounds have the structural formula (I) wherein r<sub>1</sub> is an optional double bond, R.<sup>1</sup> and R.<sup>2</sup> are selected from the group consisting of hydrogen and lower alky, or together form a cyclic substituent (II) ##STR1## wherein Q is NH, O or CH<sub>2</sub>.sub.2, and the other various substituents are as defined herein. Pharmaceutical compositions and methods for using the compounds of formula (I) to treat estrogen-dependent disorders are provided as well.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

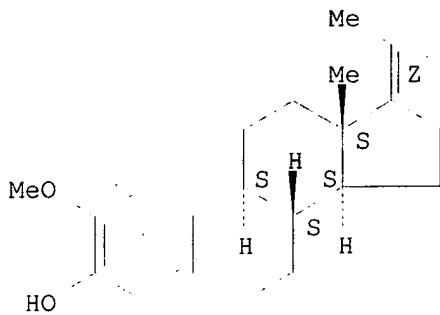
IT 229486-17-3P

(preparation of estrone sulfamates as inhibitors of estrone sulfatase)

RN 229486-17-3 USPATFULL

CN 19-Norpregna-1,3,5(10),17(20)-tetraen-3-ol, 2-methoxy-, (17Z)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.  
Double bond geometry as shown.



L37 ANSWER 4 OF 5 USPATFULL on STN  
 AN 1999:7375 USPATFULL  
 TI Steroid inhibitors of estrone sulfatase and associated pharmaceutical compositions and methods of use  
 IN Tanabe, Masato, Palo Alto, CA, United States  
     Peters, Richard H., San Jose, CA, United States  
     Chao, Wan-Ru, Sunnyvale, CA, United States  
     Shigeno, Kazuhiko, Mountain View, CA, United States  
 PA SRI International, Menlo Park, CA, United States (U.S. corporation)  
 PI US 5861388 19990119  
 AI US 1997-1601 19971231  
 RLI Division of Ser. No. US 1997-794229, filed on 29 Jan 1997, now patented,  
     Pat. No. US 5763432  
 DT Utility  
 FS Granted  
 EXNAM Primary Examiner: Dees, Jose G.; Assistant Examiner: Bodio, Barbara  
 LREP Reed, Dianne E. Bozicevic & Reed LLP  
 CLMN Number of Claims: 22  
 ECL Exemplary Claim: 1  
 DRWN No Drawings  
 LN.CNT 1778

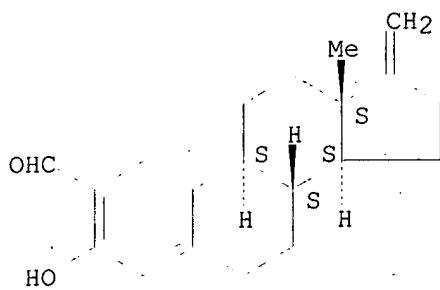
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Novel compounds useful as inhibitors of estrone sulfatase are provided.  
 The compounds have the structural formula (I) ##STR1## wherein X and Y, or Y and Z, form an oxathiazine dioxide ring or a dihydro-oxathiazine dioxide ring, and the other various substituents are as defined herein.  
 Pharmaceutical compositions and methods for using the compounds of formula (I) to treat estrogen-dependent disorders are provided as well.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT 208758-26-3P 208758-27-4P 208758-28-5P  
 208758-47-8P  
     (preparation of steroid inhibitors of estrone sulfatase)  
 RN 208758-26-3 USPATFULL  
 CN Estra-1,3,5(10)-triene-2-carboxaldehyde, 3-hydroxy-17-methylene- (9CI)  
     (CA INDEX NAME)

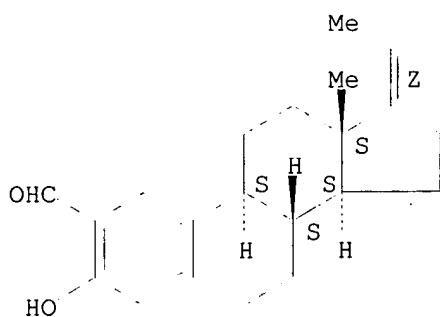
Absolute stereochemistry.



RN 208758-27-4 USPATFULL

CN 19-Norpregna-1,3,5(10),17(20)-tetraene-2-carboxaldehyde, 3-hydroxy-,  
(17Z)- (9CI) (CA INDEX NAME)

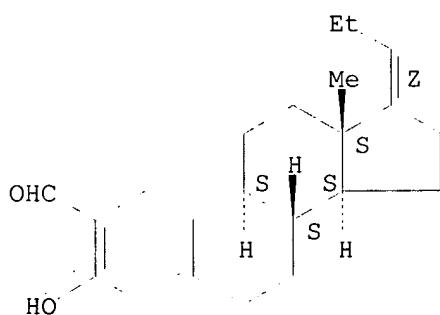
Absolute stereochemistry.  
Double bond geometry as shown.



RN 208758-28-5 USPATFULL

CN Estra-1,3,5(10)-triene-2-carboxaldehyde, 3-hydroxy-17-propylidene-, (17Z)-  
(9CI) (CA INDEX NAME)

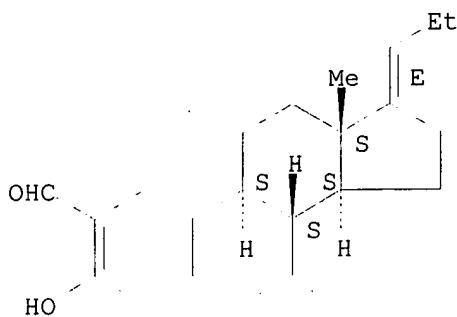
Absolute stereochemistry.  
Double bond geometry as shown.



RN 208758-47-8 USPATFULL

CN Estra-1,3,5(10)-triene-2-carboxaldehyde, 3-hydroxy-17-propylidene-, (17E)-  
(9CI) (CA INDEX NAME)

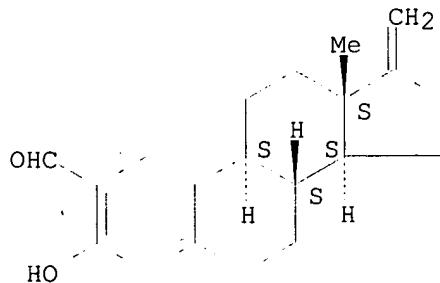
Absolute stereochemistry.  
Double bond geometry as shown.



L37 ANSWER 5 OF 5 USPATFULL on STN  
 AN 1998:65215 USPATFULL  
 TI Steriod inhibitors of estrone sulfatase and associated pharmaceutical compositions and methods of use  
 IN Tanabe, Masato, Palo Alto, CA, United States  
     Peters, Richard H., San Jose, CA, United States  
     Chao, Wan-Ru, Sunnyvale, CA, United States  
     Shigeno, Kazuhiko, Mountain View, CA, United States  
 PA SRI International, Menlo Park, CA, United States (U.S. corporation)  
 PI US 5763432 19980609  
 AI US 1997-794229 19970129 (8)  
 DT Utility  
 FS Granted  
 EXNAM Primary Examiner: Dees, Jose G.; Assistant Examiner: Badio, Barbara  
 LREP Reed, Dianne E.Bozicevic & Reed LLP  
 CLMN Number of Claims: 13  
 ECL Exemplary Claim: 1  
 DRWN No Drawings  
 LN.CNT 1700  
 CAS INDEXING IS AVAILABLE FOR THIS PATENT.  
 AB Novel compounds useful as inhibitors of estrone sulfatase are provided. The compounds have the structural formula (I) ##STR1## wherein X and Y, or Z, form an oxathiazine dioxide ring or a dihydro-oxathiazine dioxide ring, and the other various substituents are as defined herein. Pharmaceutical compositions and methods for using the compounds of formula (I) to treat estrogen-dependent disorders are provided as well.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.  
 IT 208758-26-3P 208758-27-4P 208758-28-5P  
 208758-47-8P  
     (preparation of steroid inhibitors of estrone sulfatase)  
 RN 208758-26-3 USPATFULL  
 CN Estra-1,3,5(10)-triene-2-carboxaldehyde, 3-hydroxy-17-methylene- (9CI)  
     (CA INDEX NAME)

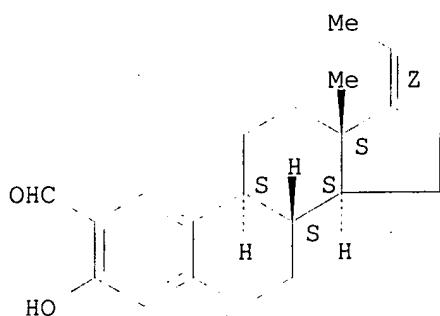
Absolute stereochemistry.



RN 208758-27-4 USPATFULL

CN 19-Norpregna-1,3,5(10),17(20)-tetraene-2-carboxaldehyde, 3-hydroxy-,  
(17Z)- (9CI) (CA INDEX NAME)

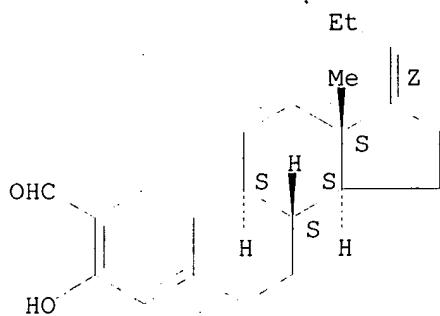
Absolute stereochemistry.  
Double bond geometry as shown.



RN 208758-28-5 USPATFULL

CN Estra-1,3,5(10)-triene-2-carboxaldehyde, 3-hydroxy-17-propylidene-, (17Z)-  
(9CI) (CA INDEX NAME)

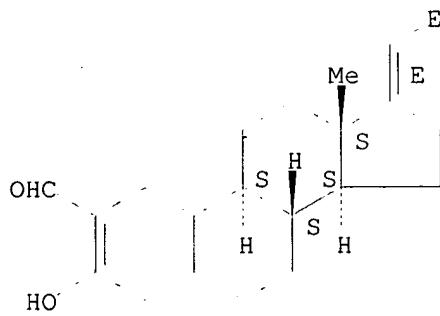
Absolute stereochemistry.  
Double bond geometry as shown.



RN 208758-47-8 USPATFULL

CN Estra-1,3,5(10)-triene-2-carboxaldehyde, 3-hydroxy-17-propylidene-, (17E)-  
(9CI) (CA INDEX NAME)

Absolute stereochemistry.  
Double bond geometry as shown.



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FILE LAST UPDATED: 19 Dec 2003 (20031219/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> d all hitstr tot 141

L41 ANSWER 1 OF 9 HCAPLUS COPYRIGHT 2003 ACS on STN  
AN 2003:719252 HCAPLUS  
DN 139:224972  
ED Entered STN: 14 Sep 2003  
TI Synthesis of 2-methoxyestradiol derivatives and uses as antiangiogenic agents  
IN Lavallee, Theresa M.; Pribluda, Victor S.; Simons, Jonathan; Mabjeesh, Nicola; Giannakakou, Paraskevi  
PA Entremed, Inc., USA  
SO PCT Int. Appl., 77 pp.  
CODEN: PIXXD2  
DT Patent  
LA English  
IC ICM A61K  
CC 2-4 (Mammalian Hormones)  
Section cross-reference(s): 32  
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2003073985	A2	20030912	WO 2003-US5898	20030227
	W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
	RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			

PRAI US 2002-361267P P 20020301

AB Compns. and methods for treating mammalian disease characterized by undesirable angiogenesis and for controlling a number of angiogenesis-related events, conditions, or substances, by administering derivs. of 2-methoxyestradiol of general formula (I) wherein the variables are defined in the specification.

ST estrogen methoxyestradiol analogs angiogenesis inhibitor VEGF DR5 HIFalpha  
 IT Apoptosis  
     (2-ME2-induced; synthesis of 2-methoxyestradiol derivs. and uses as antiangiogenic agents)  
 IT Cytokine receptors  
     RL: BSU (Biological study, unclassified); BIOL (Biological study) (DR5 (death receptor 5); synthesis of 2-methoxyestradiol derivs. and uses as antiangiogenic agents)  
 IT Transcription factors  
     RL: BSU (Biological study, unclassified); BIOL (Biological study) (HIF-1 $\alpha$  (hypoxia-inducible factor 1 $\alpha$ ); synthesis of 2-methoxyestradiol derivs. and uses as antiangiogenic agents)  
 IT Blood vessel  
     (endothelium; synthesis of 2-methoxyestradiol derivs. and uses as antiangiogenic agents)  
 IT Transcriptional regulation  
     (of HIF-1 $\alpha$ , 2-ME2-inhibited; synthesis of 2-methoxyestradiol derivs. and uses as antiangiogenic agents)  
 IT Angiogenesis  
     Angiogenesis inhibitors  
         Human  
             (synthesis of 2-methoxyestradiol derivs. and uses as antiangiogenic agents)  
 IT Estrogens  
     RL: PAC (Pharmacological activity); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)  
         (synthesis of 2-methoxyestradiol derivs. and uses as antiangiogenic agents)  
 IT 127464-60-2, Vascular Endothelial Growth Factor  
     RL: BSU (Biological study, unclassified); BIOL (Biological study)  
         (synthesis of 2-methoxyestradiol derivs. and uses as antiangiogenic agents)  
 IT 362-07-2DP, 2-Methoxyestradiol, derivs. and analogs 362-07-2P,  
     2-Methoxyestradiol  
     RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent)  
         (synthesis of 2-methoxyestradiol derivs. and uses as antiangiogenic agents)  
 IT 50-00-0, Formaldehyde, reactions 50-28-2D, Estradiol, derivs. and analogs 53-16-7, Estrone, reactions 64-18-6, Formic acid, reactions 64-19-7, Acetic acid, reactions 67-68-5, Methyl sulfoxide, reactions 68-12-2, DMF, reactions 71-36-3, 1-Butanol, reactions 75-09-2, Methylene chloride, reactions 79-37-8, Oxalyl chloride 100-39-0, Benzyl bromide 106-95-6, Allyl bromide, reactions 109-99-9, THF, reactions 111-46-6, Diethylene glycol, reactions 121-44-8, Triethylamine, reactions 141-78-6, Ethyl acetate, reactions 302-01-2, Hydrazine, reactions 362-08-3, 2-Methoxyestrone 362-08-3D, 2-Methoxyestrone, olefin analogs 584-08-7, Potassium carbonate 1157-87-5, AH3 1530-32-1, Ethyl triphenylphosphonium bromide 1779-49-3, Methyltriphenylphosphonium bromide 1779-51-7, Butyl triphenylphosphonium bromide 4111-54-0, Lithium diisopropyl amide 4784-77-4, Crotyl bromide 5815-08-7, tert-Butoxy bis(dimethylamino)methane 6228-47-3, Propyl triphenylphosphonium bromide 7447-41-8, Lithium chloride, reactions 7632-00-0, Sodium nitrite 7693-26-7, Potassium hydride 16853-85-3, Lithium aluminum hydride 17455-13-9, 18-Crown-6 17640-15-2, Methyl cyanoformate 41233-93-6, Potassium-tert-amylate 431901-79-0 431901-81-4 431901-84-7 431901-85-8 431901-89-2  
     RL: RCT (Reactant); RACT (Reactant or reagent)  
         (synthesis of 2-methoxyestradiol derivs. and uses as antiangiogenic agents)  
 IT 53-63-4P, Estra-1,3,5(10)-trien-3-ol

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
 (synthesis of 2-methoxyestradiol derivs. and uses as antiangiogenic agents)

IT 362-07-2DP, 2-Methoxyestradiol, alkyl analogs 4953-96-2P 6298-51-7P  
 6301-87-7P 6599-97-9P 7291-57-8P 10332-20-4P 26356-54-7DP, alkyl  
 derivs 26356-54-7DP, alkyl derivs. 26356-54-7P 26357-07-3DP,  
 $16\alpha$ -alkyl derivs. 26357-07-3P 32162-96-2P 34111-53-0P  
 93949-26-9P 165619-07-8P 229486-18-4P 431901-68-7P  
**431901-69-8P** 431901-70-1P 431901-71-2P **431901-72-3P**  
 431901-77-8P 431901-78-9P 431901-80-3DP, alkyl derivs.  
 431901-89-2DP, alkyl analogs 431901-90-5P 431901-91-6P 431901-92-7P  
 431901-93-8P 431901-98-3P 431901-99-4P 431902-01-1P 431902-02-2P  
 431902-03-3P 431902-04-4P 431902-05-5P 431902-06-6P 431902-09-9P  
 438044-30-5P 464924-32-1P 594873-85-5P 594873-86-6P  
**594873-87-7P**

RL: SPN (Synthetic preparation); PREP (Preparation)  
 (synthesis of 2-methoxyestradiol derivs. and uses as antiangiogenic agents)

IT **431901-69-8P 431901-72-3P 594873-87-7P**

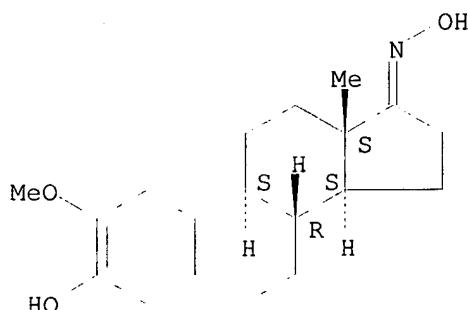
RL: SPN (Synthetic preparation); PREP (Preparation)  
 (synthesis of 2-methoxyestradiol derivs. and uses as antiangiogenic agents)

RN 431901-69-8 HCPLUS

CN Estra-1,3,5(10)-trien-17-one, 3-hydroxy-2-methoxy-, oxime (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry unknown.

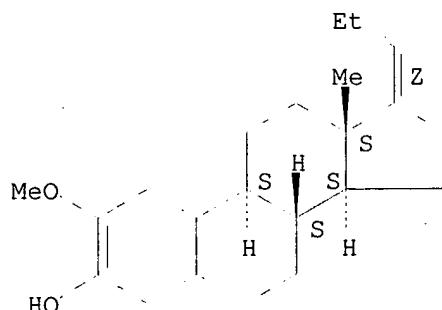


RN 431901-72-3 HCPLUS

CN Estra-1,3,5(10)-trien-3-ol, 2-methoxy-17-propylidene-, (17Z)- (9CI) (CA INDEX NAME)

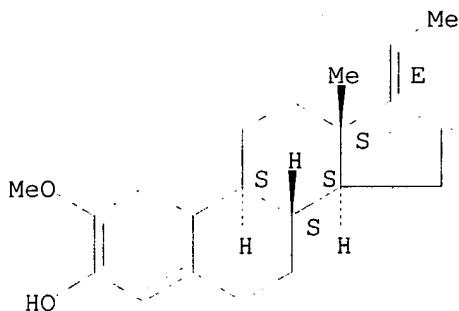
Absolute stereochemistry.

Double bond geometry as shown.



RN 594873-87-7 HCAPLUS  
 CN 19-Norpregna-1,3,5(10),17(20)-tetraen-3-ol, 2-methoxy-, (17E)- (9CI) (CA  
 INDEX NAME)

Absolute stereochemistry.  
 Double bond geometry as shown.



L41 ANSWER 2 OF 9 HCAPLUS COPYRIGHT 2003 ACS on STN  
 AN 2002:935062 HCAPLUS  
 DN 138:348841  
 ED Entered STN: 10 Dec 2002  
 TI Steroidal oxathiazine inhibitors of estrone sulfatase  
 AU Peters, Richard H.; Chao, Wan-Ru; Sato, Barbara; Shigeno, Kazuhiko;  
 Zaveri, Nurulain T.; Tanabe, Masato  
 CS Life Science Division, SRI International, Menlo Park, CA, 94025, USA  
 SO Steroids (2003), 68(1), 97-110  
 CODEN: STEDAM; ISSN: 0039-128X  
 PB Elsevier Science Inc.  
 DT Journal  
 LA English  
 CC 2-4 (Mammalian Hormones)  
 Section cross-reference(s): 1, 7  
 OS CASREACT 138:348841  
 AB The presence of estrone sulfatase in breast tumors and the high levels of circulating estrone sulfate may contribute the major portion of estrogen synthesized locally in breast tissues through conversion of estrone sulfate to estrone by the enzyme. Using inhibitors of estrone sulfatase for the treatment of estrogen-dependent (estrogen receptor pos., ER+) breast cancer could be a very effective therapeutic strategy for the treatment of estrogen-dependent breast tumors in postmenopausal women. Therefore, the authors designed and synthesized several steroidal 2',3'-oxathiazines that inhibit estrone sulfatase and have greatly reduced estrogenic side effects. The authors' in vitro studies indicate that the oxathiazine compds. have inhibitory activity on estrone sulfatase in MCF-7 human breast cancer cells. These estrone sulfatase inhibitors (ESIs) also inhibit the growth of MCF-7 cells induced by estrone sulfate. In addition, the authors' in vivo expts. demonstrate that the authors' ESIs have moderate antitumor activity against MCF-7 breast cancer xenografts in Balb/c athymic nude mice. The synthesis and biol. activity of a number of these unique steroidal ESIs are described.  
 ST estrone sulfatase inhibitor breast cancer proliferation inhibition  
 IT Cell proliferation  
     (inhibition; steroid oxathiazine inhibitors of estrone sulfatase in relation to synthesis and biol. activity in MCF-7 cells)  
 IT Antitumor agents  
 Double bond  
 Human  
 Mammary gland, neoplasm  
     (steroideal oxathiazine inhibitors of estrone sulfatase in relation to

synthesis and biol. activity in MCF-7 cells)  
IT 53-16-7, Estrone, biological studies 481-97-0, Estrone sulfate  
RL: ADV (Adverse effect, including toxicity); BSU (Biological study, unclassified); BIOL (Biological study)  
(steroideal oxathiazine inhibitors of estrone sulfatase in relation to synthesis and biol. activity in MCF-7 cells)

7732-18-5, Water, biological studies 9001-78-9, Alkaline phosphatase 59298-96-3, Sulfatase, estrone  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(steroideal oxathiazine inhibitors of estrone sulfatase in relation to synthesis and biol. activity in MCF-7 cells)

208758-16-1P 208758-17-2P 208758-20-7P 208758-21-8P 208758-23-0P  
208758-25-2P 208758-33-2P 208758-34-3P 208758-35-4P 208758-36-5P  
208758-37-6P 208758-38-7P 208758-39-8P 208758-41-2P 208758-43-4P  
208758-48-9P 208758-52-5P 208758-54-7P 519039-19-1P 519039-26-0P  
519039-29-3P 519039-31-7P 519039-33-9P 519039-37-3P  
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)  
(steroideal oxathiazine inhibitors of estrone sulfatase in relation to synthesis and biol. activity in MCF-7 cells)

6599-97-9P 13879-55-5P 13879-56-6P 31559-62-3P 123715-79-7P  
137352-12-6P 208758-18-3P 208758-19-4P 208758-22-9P 208758-24-1P  
**208758-26-3P 208758-27-4P 208758-28-5P**  
208758-29-6P 208758-30-9P 208758-31-0P 208758-32-1P 208758-40-1P  
208758-42-3P **208758-47-8P** 208758-51-4P 208758-53-6P  
519039-17-9P 519039-25-9P 519039-28-2P 519039-30-6P 519039-34-0P  
519039-35-1P 519039-36-2P  
RL: PRP (Properties); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
(steroideal oxathiazine inhibitors of estrone sulfatase in relation to synthesis and biol. activity in MCF-7 cells)

50-28-2, Estra-1,3,5(10)-triene-3,17-diol (17 $\beta$ )-, reactions  
1189-71-5, Chlorosulfonyl isocyanate 4736-62-3 4954-12-5 18162-48-6,  
Tert-Butyldimethyl chlorosilane 34111-53-0 64215-82-3 99898-93-8  
116627-20-4 120574-27-8 120574-28-9 185910-40-1 208758-46-7  
208758-50-3 229486-09-3 229486-13-9 519039-16-8 519039-27-1  
RL: RCT (Reactant); RACT (Reactant or reagent)  
(steroideal oxathiazine inhibitors of estrone sulfatase in relation to synthesis and biol. activity in MCF-7 cells)

RE.CNT 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

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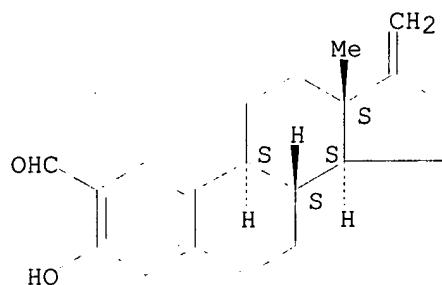
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 (26) Tanabe, M; US 6046186 2000 HCPLUS  
 (27) Yue, W; J Steroid Biochem Mol Biol 1993, V44, P4  
 IT 208758-26-3P 208758-27-4P 208758-28-5P  
 208758-47-8P

RL: PRP (Properties); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
 (steroidal oxathiazine inhibitors of estrone sulfatase in relation to synthesis and biol. activity in MCF-7 cells)

RN 208758-26-3 HCPLUS

CN Estra-1,3,5(10)-triene-2-carboxaldehyde, 3-hydroxy-17-methylene- (9CI)  
 (CA INDEX NAME)

Absolute stereochemistry.

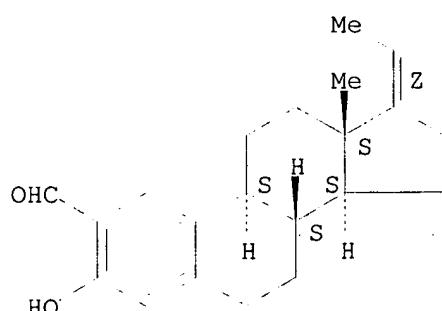


RN 208758-27-4 HCPLUS

CN 19-Norpregna-1,3,5(10),17(20)-tetraene-2-carboxaldehyde, 3-hydroxy-, (17Z)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.

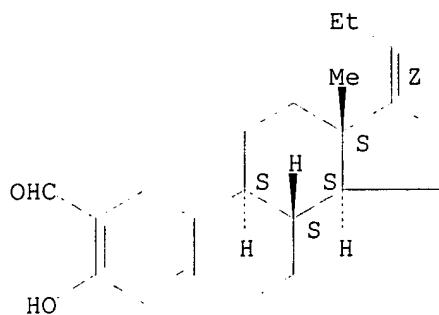


RN 208758-28-5 HCPLUS

CN Estra-1,3,5(10)-triene-2-carboxaldehyde, 3-hydroxy-17-propylidene-, (17Z)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.

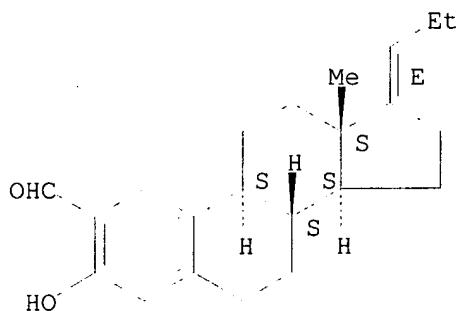


RN 208758-47-8 HCAPLUS

CN Estra-1,3,5(10)-triene-2-carboxaldehyde, 3-hydroxy-17-propylidene-, (17E)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.



L41 ANSWER 3 OF 9 HCAPLUS COPYRIGHT 2003 ACS on STN

AN 2002:888569 HCAPLUS

DN 137:370278

ED Entered STN: 22 Nov 2002

TI Preparation of substituted pregn-1,3,5(10)-triene derivatives for pharmaceutical use

IN Hesse, Robert Henry; Setty, Sundara Katugam Srinivasasetty; Pechet, Maurice Murdoch; Gile, Michael

PA Marsden, John Christopher, UK; Research Institute for Medicine and Chemistry Inc.

SO PCT Int. Appl., 28 pp.  
CODEN: PIXXD2

DT Patent

LA English

IC ICM A61K031-56

ICS A61K031-575; C07J041-00; A61P035-00

CC 32-5 (Steroids)

Section cross-reference(s): 1, 2, 63

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002092100	A1	20021121	WO 2002-GB2210	20020513
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU,				

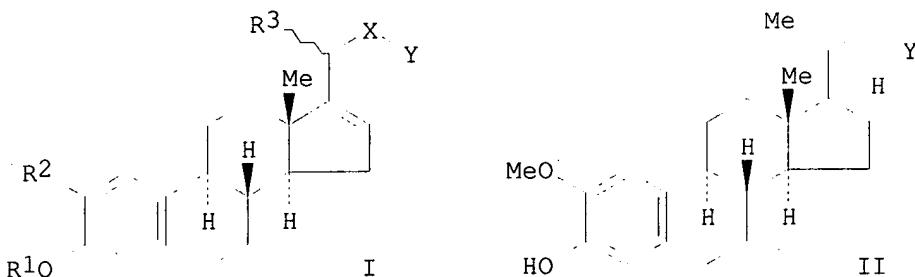
TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH,  
 CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR,  
 BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRAI US 2001-290013P P 20010511

OS MARPAT 137:370278

GI



AB Pregna-1,3,5(10)-triene derivs., such as I [R1 = H, hydroxy protecting group; R2 = OH, CHO, alkoxy, alkenyl, alkyl, etc.; R3 =  $\alpha$ -,  $\beta$ -Me; X = C1-3 alkylene group, bond; Y = C(R4)(R5)NR6R7; R4, R5 = H, alkyl, alkenyl and alkynyl groups, such that the total carbon content of R4 and R5 does not exceed three atoms; R6 = H, aliphatic or araliph. organic group, acyl, etc.; C16-C17 = saturated, unsatd.], were prepared for a variety of therapeutic uses, such as modulating cell activity, including antiproliferative and antiangiogenic effects. Thus, pregnna-1,3,5(10)-triene derivs. II (Y = NH<sub>2</sub>, NHCOMe) were prepared via a multistep synthetic series starting from 2-methoxy-3-[[(tris(1-methylethyl)silyl)oxy]-estra-1,3,5(10)-trien-17-one and ethyltriphenylphosphonium bromide.

Pharmaceutical compns. of the prepared compds. were discussed, but specific pharmaceutical activity testing data was not presented.

ST norpregnatriene prepn antiproliferative antiangiogenic agent

IT Mental disorder

(cognitive, treatment; preparation of substituted pregnna-1,3,5(10)-triene derivs. for a variety of therapeutic uses)

IT Blood coagulation

Cognition

(disorder, treatment; preparation of substituted pregnna-1,3,5(10)-triene derivs. for a variety of therapeutic uses)

IT Transplant and Transplantation

(graft-vs.-host reaction, treatment; preparation of substituted pregnna-1,3,5(10)-triene derivs. for a variety of therapeutic uses)

IT Anti-inflammatory agents

Anticholesteremic agents

Antitumor agents

Cognition enhancers

Contraceptives

Immunomodulators

(preparation of substituted pregnna-1,3,5(10)-triene derivs. for a variety of therapeutic uses)

IT Arthritis

(psoriatic arthritis, treatment; preparation of substituted pregnna-1,3,5(10)-triene derivs. for a variety of therapeutic uses)

IT Mental disorder

(senile psychosis, treatment; preparation of substituted pregnna-1,3,5(10)-triene derivs. for a variety of therapeutic uses)

IT   Asthma  
 Autoimmune disease  
 Bone, disease  
 Hypercholesterolemia  
 Hyperplasia  
 Hypertension  
 Inflammation  
 Neoplasm  
 Rheumatoid arthritis  
 Skin, disease  
 Transplant rejection  
 (treatment; preparation of substituted pregnna-1,3,5(10)-triene derivs. for a variety of therapeutic uses)

IT   4736-60-1, Ethyltriphenylphosphonium iodide   305812-67-3  
 RL: RCT (Reactant); RACT (Reactant or reagent)  
 (preparation of substituted pregnna-1,3,5(10)-triene derivs. for a variety of therapeutic uses)

IT   229486-17-3P   305812-87-7P   305812-99-1P   372952-47-1P  
 372952-49-3P   372952-50-6P   475486-81-8P   475486-82-9P   475486-83-0P  
 475486-84-1P  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
 (preparation of substituted pregnna-1,3,5(10)-triene derivs. for a variety of therapeutic uses)

IT   475486-79-4P   475486-80-7P  
 RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
 (preparation of substituted pregnna-1,3,5(10)-triene derivs. for a variety of therapeutic uses)

RE.CNT 4   THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

- (1) Christopher, M; WO 0068246 A 2000 HCPLUS
- (2) Christopher, M; WO 0185755 A 2001 HCPLUS
- (3) Cushman, M; JOURNAL OF MEDICINAL CHEMISTRY 1995, V38(12), P2041 HCPLUS
- (4) Jacques, P; US 3291690 A 1966

IT   229486-17-3P

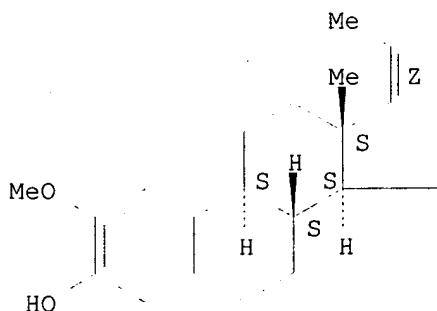
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
 (preparation of substituted pregnna-1,3,5(10)-triene derivs. for a variety of therapeutic uses)

RN   229486-17-3   HCPLUS

CN   19-Norpregna-1,3,5(10),17(20)-tetraen-3-ol, 2-methoxy-, (17Z)- (9CI)   (CA INDEX NAME)

Absolute stereochemistry.

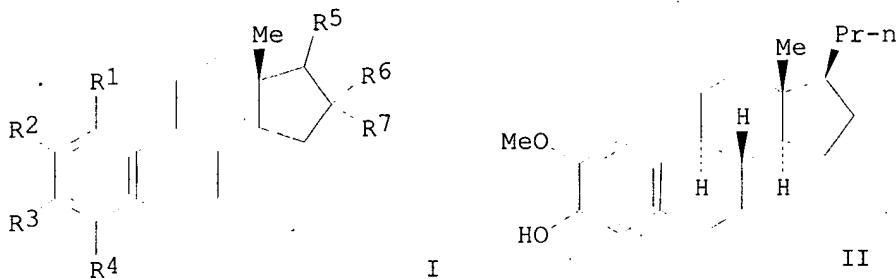
Double bond geometry as shown.



DN 137:47357  
 ED Entered STN: 28 Jun 2002  
 TI Preparation of 2-methoxyestradiol derivatives as antiangiogenic agents  
 IN Agoston, Gregory E.; Shah, Jamshed H.; Hunsucker,  
   Kimberly A.; Pribluda, Victor S.; Lavallee, Theresa  
   M.; Green, Shawn J.; Herbstritt, Christopher J.;  
   Zhan, Xiaoguo H.; Treston, Anthony M.  
 PA USA  
 SO U.S. Pat. Appl. Publ., 37 pp., Cont.-in-part of U. S. Ser. No. 933,894.  
   CODEN: USXXCO  
 DT Patent  
 LA English  
 IC ICM C07J041-00  
   ICS C07J043-00; C07J001-00; A61K031-704; A61K031-58; A61K031-56;  
     C07C247-00; A61K031-655; C07J009-00  
 NCL 552544000  
 CC 32-3 (Steroids)  
   Section cross-reference(s): 1  
 FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2002082433	A1	20020627	US 2001-939208	20010824
PRAI	US 2000-641327	A2	20000818		
	US 2000-253385P	P	20001127		
	US 2000-255302P	P	20001213		
	US 2001-278250P	P	20010323		
	US 2001-933894	A2	20010821		

OS MARPAT 137:47357  
 GI



AB 2-Methoxyestradiol derivs. of formula I [R1, R4 = H, halo, CN, alkyl, OH, NH2, etc.; R2 = N3, CN, OMe, alkenyl, alkynyl, alkoxy, NH2, etc.; R3 = OH, OAc; R5 = alkyl, alkenyl, (di)alkylamino, OH, alkylene, etc.; R6, R7 = H, alkyl, alkenyl, alkynyl, halo, etc.] are prepared for treating mammalian disease characterized by undesirable angiogenesis. Thus, II was prepared from 2-methoxyestradiol and propyltriphenylphosphonium bromide. The IC50 of II against MDA-MB-231 breast tumor cells was 51.31  $\mu$ M.  
 ST methoxyestradiol deriv prepn antiangiogenic; estradiol deriv prepn antiangiogenic; antitumor methoxyestradiol deriv prepn; antimitotic methoxyestradiol deriv prepn  
 IT Structure-activity relationship  
   (antitumor; preparation of 2-methoxyestradiol derivs. as antiangiogenic agents)  
 IT Mitosis  
   (inhibitors; preparation of 2-methoxyestradiol derivs. as antiangiogenic agents)  
 IT Angiogenesis inhibitors

## Antitumor agents

Human

Mammary gland, neoplasm

Neoplasm

(preparation of 2-methoxyestradiol derivs. as antiangiogenic agents)

IT 362-07-2, 2-Methoxyestradiol

RL: PAC (Pharmacological activity); RCT (Reactant); BIOL (Biological study); RACT (Reactant or reagent)

(preparation of 2-methoxyestradiol derivs. as antiangiogenic agents)

IT 53-63-4P, Estra-1,3,5(10)-trien-3-ol 6301-87-7P 431901-72-3P

431901-73-4P 431901-75-6P 431901-77-8P 431901-91-6P

RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

(preparation of 2-methoxyestradiol derivs. as antiangiogenic agents)

IT 1818-12-8P 4953-96-2P 6298-51-7P 6599-97-9P 7291-57-8P

10332-20-4P 32162-96-2P 41259-43-2P 94440-60-5P 165619-07-8P

165881-61-8P 229486-18-4P 431901-68-7P 431901-69-8P

431901-70-1P 431901-71-2P 431901-74-5P 431901-78-9P 431901-87-0P

431901-90-5P 431901-92-7P 431901-93-8P 431901-94-9P 431901-95-0P

431901-96-1P 431901-97-2P 431901-98-3P 431901-99-4P 431902-00-0P

431902-01-1P 431902-02-2P 431902-03-3P 431902-04-4P 431902-05-5P

431902-06-6P 431902-07-7P 431902-08-8P 431902-09-9P 438044-29-2P

438044-30-5P 438044-35-0P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of 2-methoxyestradiol derivs. as antiangiogenic agents)

IT 53-16-7, Estrone, reactions 106-95-6, Allyl bromide, reactions

1779-51-7, Butyltriphenylphosphonium bromide 4784-77-4, Crotyl bromide

5815-08-7 6228-47-3, Propyltriphenylphosphonium bromide

RL: RCT (Reactant); RACT (Reactant or reagent)

(preparation of 2-methoxyestradiol derivs. as antiangiogenic agents)

IT 26356-54-7P 26357-07-3P 93949-26-9P 431901-79-0P 431901-81-4P

431901-82-5P 431901-83-6P 431901-84-7P 431901-85-8P 431901-89-2P

438044-31-6P 438044-32-7P 438044-33-8P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of 2-methoxyestradiol derivs. as antiangiogenic agents)

IT 431901-72-3P 431901-75-6P

RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

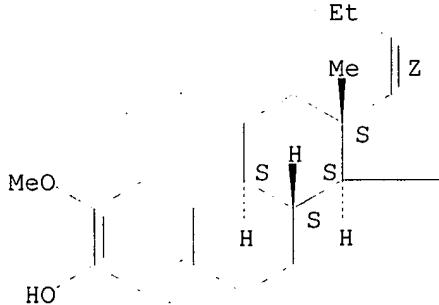
(preparation of 2-methoxyestradiol derivs. as antiangiogenic agents)

RN 431901-72-3 HCAPLUS

CN Estra-1,3,5(10)-trien-3-ol, 2-methoxy-17-propylidene-, (17Z)- (9CI) (CA INDEX NAME)

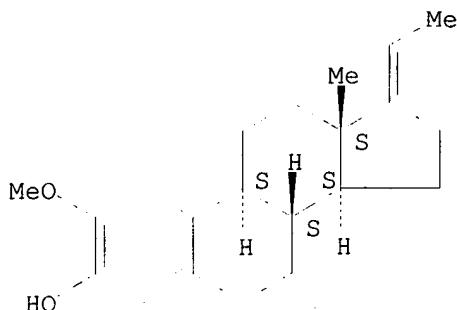
Absolute stereochemistry.

Double bond geometry as shown.



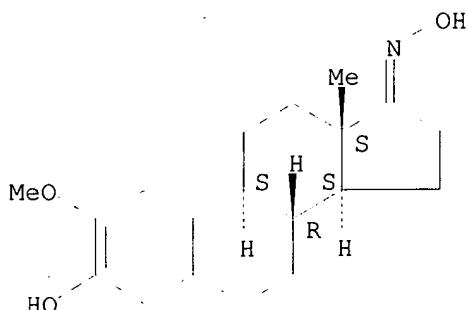
RN 431901-75-6 HCPLUS  
 CN 19-Norpregna-1,3,5(10),17(20)-tetraen-3-ol, 2-methoxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry.  
 Double bond geometry unknown.



IT 431901-69-8P  
 RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
 (preparation of 2-methoxyestradiol derivs. as antiangiogenic agents)  
 RN 431901-69-8 HCPLUS  
 CN Estra-1,3,5(10)-trien-17-one, 3-hydroxy-2-methoxy-, oxime (9CI) (CA INDEX NAME)

Absolute stereochemistry.  
 Double bond geometry unknown.

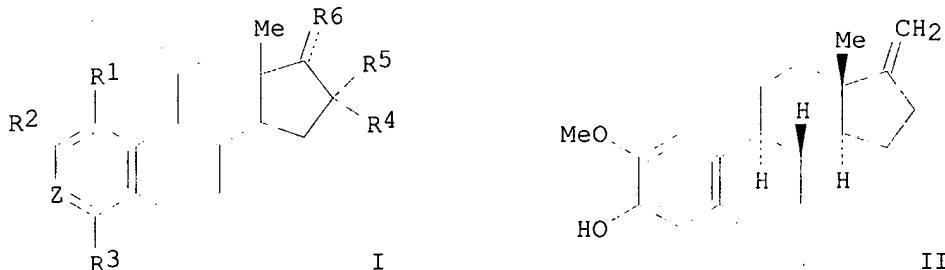


L41 ANSWER 5 OF 9 HCPLUS COPYRIGHT 2003 ACS on STN  
 AN 2002:408687 HCPLUS  
 DN 137:6309  
 ED Entered STN: 31 May 2002  
 TI Preparation of 2-methoxyestradiol analogs as antiangiogenic agents  
 IN Agoston, Gregory; Shah, Jamshed H.; Hunsucker,  
 Kimberly A.; Pribluda, Victor; Lavallee, Theresa M.  
 ; Green, Shawn J.; Herbstritt, Christopher J.;  
 Zhan, Xiaoguo H.; Treston, Anthony  
 PA Entremed, Inc., USA  
 SO PCT Int. Appl., 86 pp.  
 CODEN: PIXXD2  
 DT Patent  
 LA English  
 IC ICM C07J001-00  
 CC 32-3 (Steroids)

Section cross-reference(s): 1, 2, 63

FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002042319	A2	20020530	WO 2001-US26490	20010824
	WO 2002042319	A3	20030313		
	W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
	RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
	AU 2001088386	A5	20020603	AU 2001-88386	20010824
	EP 1343803	A2	20030917	EP 2001-968112	20010824
	R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR			
PRAI	US 2000-253385P	P	20001127		
	US 2000-255302P	P	20001213		
	US 2001-278250P	P	20010323		
	US 2001-933894	A	20010821		
	WO 2001-US26490	W	20010824		
OS	MARPAT	137:6309			
GI					



AB 2-Methoxyestradiol analogs, such as I [R1, R3 = H, halo, CN, alkyl, OH, CH<sub>2</sub>OH, NH<sub>2</sub>, alkylamino; R2 = N<sub>3</sub>, CN, C.tplbond.CR, C=CHR, C.tplbond.CH, OR, amino; R = H, alkyl; Z = COH, COAc; dashed bond = single bond or double bond; R6 = H, OH, O, oxime, amino, alkyl, alkenyl; R4, R5 = H, alkyl, alkenyl, alkynyl], were prepared for treating mammalian disease characterized by undesirable angiogenesis. Thus, 2-methoxyestradiol analog II was prepared by the reaction of methyltriphenylphosphonium bromide and 2-methoxyestrone. In vitro evaluation against MDA-MB-231 breast tumor cells and HUVEC endothelial cells, II showed IC<sub>50</sub> 0.24±0 and 0.19±0.19 resp.

ST methoxyestradiol deriv prep antiangiogenic antitumor; estradiol methoxy deriv prep antiangiogenic antitumor

IT Cell proliferation

(inhibition; preparation of 2-methoxyestradiol derivs. as antiangiogenic agents)

IT Mammary gland, neoplasm

(inhibitors; preparation of 2-methoxyestradiol derivs. as antiangiogenic agents)

IT Antitumor agents

(mammary gland; preparation of 2-methoxyestradiol derivs. as antiangiogenic agents)

IT Angiogenesis inhibitors

Human  
 (preparation of 2-methoxyestradiol derivs. as antiangiogenic agents)

IT Estrogens  
 RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

(preparation of 2-methoxyestradiol derivs. as antiangiogenic agents)

IT 53-63-4P, Estra-1,3,5(10)-trien-3-ol 431901-72-3P 431901-73-4P  
 431901-75-6P 431901-77-8P 431901-83-6P 431901-89-2P  
 431901-91-6P  
 RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

(preparation of 2-methoxyestradiol derivs. as antiangiogenic agents)

IT 1818-12-8P 4953-96-2P 6298-51-7P 6301-87-7P 6599-97-9P  
 7291-57-8P 10332-20-4P 32162-96-2P 41259-43-2P 94440-60-5P  
 165619-07-8P 165881-61-8P 192062-02-5P 229486-18-4P 431901-68-7P  
**431901-69-8P** 431901-70-1P 431901-71-2P 431901-74-5P  
 431901-76-7P 431901-78-9P 431901-82-5P 431901-84-7P 431901-86-9P  
 431901-87-0P 431901-88-1P 431901-92-7P 431901-93-8P 431901-94-9P  
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 431902-00-0P 431902-01-1P 431902-02-2P 431902-03-3P 431902-04-4P  
 431902-05-5P 431902-06-6P 431902-07-7P 431902-08-8P 431902-09-9P  
 RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of 2-methoxyestradiol derivs. as antiangiogenic agents)

IT 53-16-7, Estrone, reactions 64-18-6, Formic acid, reactions 100-39-0,  
 Benzyl bromide 106-95-6, Allyl bromide, reactions 362-07-2,  
 2-Methoxyestradiol 1530-32-1, Ethyl triphenylphosphonium bromide  
 1779-49-3, Methyl triphenylphosphonium bromide 1779-51-7, Butyl  
 triphenylphosphonium bromide 4784-77-4, Crotyl bromide 5815-08-7,  
 tert-Butoxy bis(dimethylamino)methane 6228-47-3, Propyl  
 triphenylphosphonium bromide 17640-15-2, Methyl cyanoformate  
 RL: RCT (Reactant); RACT (Reactant or reagent)

(preparation of 2-methoxyestradiol derivs. as antiangiogenic agents)

IT 26356-54-7P 26357-07-3P 93949-26-9P 431901-79-0P 431901-80-3P  
 431901-81-4P 431901-85-8P 431901-90-5P  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

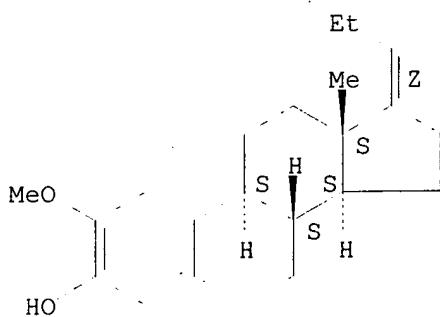
(preparation of 2-methoxyestradiol derivs. as antiangiogenic agents)

IT **431901-72-3P** **431901-75-6P**  
 RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

(preparation of 2-methoxyestradiol derivs. as antiangiogenic agents)

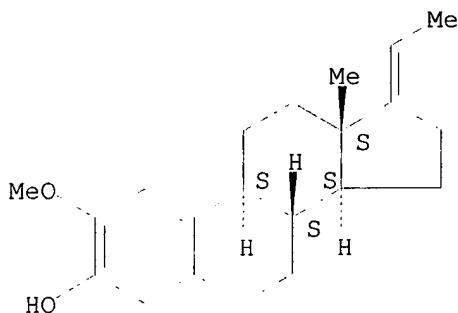
RN 431901-72-3 HCAPLUS  
 CN Estra-1,3,5(10)-trien-3-ol, 2-methoxy-17-propylidene-, (17Z)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.  
 Double bond geometry as shown.



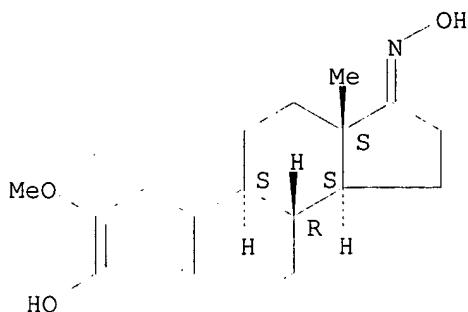
RN 431901-75-6 HCAPLUS  
CN 19-Norpregna-1,3,5(10),17(20)-tetraen-3-ol, 2-methoxy- (9CI) (CA INDEX  
NAME)

Absolute stereochemistry.  
Double bond geometry unknown.



IT 431901-69-8P  
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
RN 431901-69-8 HCAPLUS  
CN Estra-1,3,5(10)-trien-17-one, 3-hydroxy-2-methoxy-, oxime (9CI) (CA INDEX NAME)

Absolute stereochemistry.  
Double bond geometry unknown.



L41 ANSWER 6 OF 9 HCAPLUS COPYRIGHT 2003 ACS on STN  
AN 2001:833342 HCAPLUS  
DN 135:358085

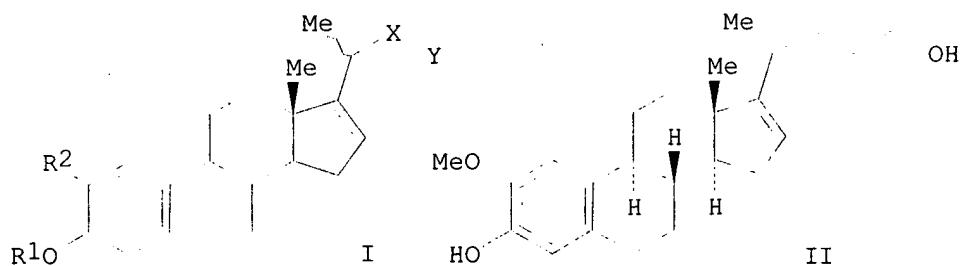
ED Entered STN: 16 Nov 2001  
 TI Preparation of 2-substituted pregn-1,3,5(10)-triene and chola-1,3,5(10)-triene derivatives with antiproliferative and antiangiogenic activity  
 IN Hesse, Robert Henry; Setty, Sundara Katugam Srinivasasetty; Pechet, Maurice Murdoch; Gile, Michael  
 PA Marsden, John Christopher, UK; Research Institute for Medicine and Chemistry Inc.  
 SO PCT Int. Appl., 40 pp.  
 CODEN: PIXXD2  
 DT Patent  
 LA English  
 IC ICM C07J041-00  
 ICS A61K031-57; C07J009-00; C07J013-00; C07J051-00; A61K031-575;  
 A61P005-30; A61P035-00  
 CC 32-5 (Steroids)  
 Section cross-reference(s): 1, 63

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001085755	A1	20011115	WO 2001-GB2103	20010511
	W: AE, AG, AL, AM, AT, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EE, EE, ES, FI, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	EP 1287017	A1	20030305	EP 2001-928120	20010511
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
	JP 2003532737	T2	20031105	JP 2001-582354	20010511
	NO 2002005392	A	20030109	NO 2002-5392	20021111
	US 2003158167	A1	20030821	US 2003-275257	20030313
PRAI	US 2000-203462P	P	20000511		
	WO 2001-GB2103	W	20010511		

OS MARPAT 135:358085

GI



AB Compds. of formula I [R1 = H, protecting group; R2 = OH, alkoxy, CHO, alkynyl, etc.; X = alkylene, bond; Y = CHO, (substituted) CH2OH, etc.] are prepared which exhibit potent cell modulating activity, including antiproliferative and antiangiogenic effects. Thus, 2-methoxy-3-triisopropylsilyloxy-19-norpregn-1,3,5(10),17(20)Z-tetraene (preparation given) is reacted with Me acrylate, reduced with LiAlH4, and desilylated with TBAF to give II.  
 ST pregnatriene deriv prepns antiproliferative antiangiogenic; cholatriene

deriv prepn antiproliferative antiangiogenic; antiproliferative pregnatriene cholatriene deriv; antiangiogenic pregnatriene cholatriene deriv

IT Angiogenesis inhibitors  
Antitumor agents  
(preparation of 2-substituted pregnatriene and cholatriene derivs. with antiproliferative and antiangiogenic activity)

IT Proliferation inhibition  
(proliferation inhibitors; preparation of 2-substituted pregnatriene and cholatriene derivs. with antiproliferative and antiangiogenic activity)

IT 372952-25-5P 372952-27-7P 372952-29-9P 372952-30-2P  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)  
(preparation of 2-substituted pregnatriene and cholatriene derivs. with antiproliferative and antiangiogenic activity)

IT 372952-23-3P 372952-24-4P 372952-28-8P 372952-31-3P 372952-32-4P  
372952-33-5P 372952-34-6P 372952-35-7P 372952-36-8P 372952-37-9P  
372952-38-0P 372952-39-1P 372952-40-4P 372952-41-5P 372952-42-6P  
372952-43-7P 372952-44-8P 372952-45-9P  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
(preparation of 2-substituted pregnatriene and cholatriene derivs. with antiproliferative and antiangiogenic activity)

IT 96-33-3, Methyl acrylate 305812-67-3 372952-58-4  
RL: RCT (Reactant); RACT (Reactant or reagent)  
(preparation of 2-substituted pregnatriene and cholatriene derivs. with antiproliferative and antiangiogenic activity)

IT 229486-17-3P 305812-87-7P 305812-89-9P 305812-91-3P  
305812-97-9P 372952-46-0P 372952-47-1P 372952-48-2P 372952-49-3P  
372952-50-6P 372952-51-7P 372952-52-8P 372952-53-9P 372952-54-0P  
372952-55-1P 372952-56-2P 372952-57-3P  
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
(preparation of 2-substituted pregnatriene and cholatriene derivs. with antiproliferative and antiangiogenic activity)

RE.CNT 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

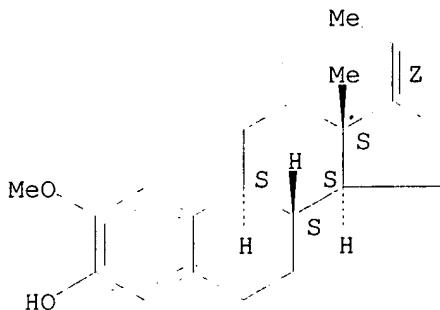
- (1) Cushman, M; JOURNAL OF MEDICINAL CHEMISTRY 1995, V38(12), P2041 HCPLUS
- (2) Marsden, J; WO 0068246 A 2000 HCPLUS
- (3) Mitsubishi Chemical Industries Co Ltd; JP 54112849 A HCPLUS
- (4) Mitsubishi Chemical Industries Co Ltd; JP 54112850 A HCPLUS
- (5) Mitsubishi Chemical Industries Co Ltd; JP 54117454 A HCPLUS
- (6) Mitsubishi Chemical Industries Co Ltd; JP 54117455 A HCPLUS
- (7) Mitsubishi Chemical Industries Co Ltd; JP 54117456 A HCPLUS
- (8) Mitsubishi Chemical Industries Co Ltd; JP 54112849 A 1979 HCPLUS
- (9) Mitsubishi Chemical Industries Co Ltd; JP 54112850 A 1979 HCPLUS
- (10) Mitsubishi Chemical Industries Co Ltd; JP 54117454 A 1979 HCPLUS
- (11) Mitsubishi Chemical Industries Co Ltd; JP 54117455 A 1979 HCPLUS
- (12) Mitsubishi Chemical Industries Co Ltd; JP 54117456 A 1979 HCPLUS
- (13) Mitsubishi Chemical Industries Co Ltd; PATENT ABSTRACTS OF JAPAN 1979, V003(133), PC-063
- (14) Mitsubishi Chemical Industries Co Ltd; PATENT ABSTRACTS OF JAPAN 1979, V003(133), PC-063
- (15) Ruggieri, P; US 3562260 A 1971 HCPLUS

IT 229486-17-3P  
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
(preparation of 2-substituted pregnatriene and cholatriene derivs. with antiproliferative and antiangiogenic activity)

RN 229486-17-3 HCPLUS

CN 19-Norpregna-1,3,5(10),17(20)-tetraen-3-ol, 2-methoxy-, (17Z)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.  
Double bond geometry as shown.

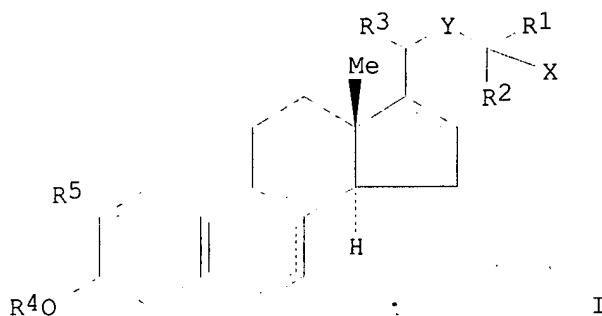


L41 ANSWER 7 OF 9 HCAPLUS COPYRIGHT 2003 ACS on STN  
 AN 2000:814500 HCAPLUS  
 DN 133:350395  
 ED Entered STN: 21 Nov 2000  
 TI Synthesis of cholestan compounds with a c17-alkyl side chain and an aromatic A-ring for use in cell modulating therapy  
 IN Hesse, Robert Henry; Setty, Sundara Katugam Srinivasasetty; Ramgopal, Malathi; Kugabaluusoorian, Sanga  
 PA Marsden, John, Christopher, UK; Research Institute for Medicine and Chemistry Inc.  
 SO PCT Int. Appl., 75 pp.  
 CODEN: PIXXD2  
 DT Patent  
 LA English  
 IC ICM C07J009-00  
 ICS C07J041-00; A61K031-575; C07J051-00; A61P017-02; A61P019-08;  
 A61P037-06; A61P029-00; A61P035-00; A61P021-00; A61P009-10;  
 A61P005-20; A61P017-00; A61P009-12; A61P019-02; A61P011-06;  
 A61P025-28; A61P015-18; A61P007-02; A61P003-06  
 CC 32-7 (Steroids)  
 Section cross-reference(s): 1, 2

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2000068246	A1	20001116	WO 2000-GB1813	20000511
	W: AE, AG, AL, AM, AT, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EE, EE, ES, FI, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP	1179005	A1	20020213	EP 2000-927569	20000511
EP	1179005	B1	20031119		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
ZA	2001009272	A	20021128	ZA 2001-9272	20011109
NO	2001005520	A	20020109	NO 2001-5520	20011112
PRAI	GB 1999-10934	A	19990511		
	WO 2000-GB1813	W	20000511		

OS MARPAT 133:350395  
 GI



AB Synthesis of cholestane compds. (I) [R1 and R2, which may be the same or different, = alkyl, alkenyl, alkynyl; R3 = Me having  $\alpha$ - or  $\beta$ -configuration; R4 = H or an etherifying or esterifying group; R5 = H, OH, alkoxy; X = OR4, wherein R4 is as defined above, or NR6R7 wherein R6 = H, aliphatic or araliph. organic group, acyl group comprising aliphatic, araliph. or aryl organic group linked to the nitrogen atom by way of a carbonyl group; R7 = H, alkyl; Y = (un)substituted alkylene, alkenylene, alkynylene; dotted lines signify that double bonds may be present at the 16(17)-position and/or either at the 6(7)- and 8(9)-positions or at the 7(8)-position] is disclosed for modulation of cell growth and differentiation, while having low calcemic activity. Thus, I [R1, R2 = Me; R3 =  $\alpha$ -Me; R4, R5 = H; X = NHAc; Y = (CH2)4;  $\Delta$ 16 double bond] is prepared by reaction of 3-triisopropylsilyloxy-19-norchol-1,3,5(10),16-tetraene-24-bromide with acetonitrile followed by reduction of nitrile to amine, methylation of amine with Me lithium, acetylation of the amino with acetic anhydride and desilylation with TBAF.

ST cholestane analog prepn cell growth modulation differentiation; low calcemic activity cholestane analog

IT Steroids, preparation

Steroids, preparation

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(aromatic; synthesis of cholestane compds. with a c17-alkyl side chain and an aromatic A-ring for use in cell modulating therapy)

IT Transplant and Transplantation

(host-vs.-graft reaction; synthesis of cholestane compds. with a c17-alkyl side chain and an aromatic A-ring for use in cell modulating therapy)

IT Arthritis

(psoriatic arthritis; synthesis of cholestane compds. with a c17-alkyl side chain and an aromatic A-ring for use in cell modulating therapy)

IT Hyperparathyroidism

(secondary; synthesis of cholestane compds. with a c17-alkyl side chain and an aromatic A-ring for use in cell modulating therapy)

IT Mental disorder

(senile psychosis; synthesis of cholestane compds. with a c17-alkyl side chain and an aromatic A-ring for use in cell modulating therapy)

IT Heart, disease

(spondylitic; synthesis of cholestane compds. with a c17-alkyl side chain and an aromatic A-ring for use in cell modulating therapy)

IT Aromatic hydrocarbons, preparation

Aromatic hydrocarbons, preparation

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use);

BIOL (Biological study); PREP (Preparation); USES (Uses)  
 (steroids; synthesis of cholestane compds. with a c17-alkyl side chain  
 and an aromatic A-ring for use in cell modulating therapy)

IT Anti-inflammatory agents  
 Antitumor agents  
 Asthma  
 Autoimmune disease  
 Blood coagulation  
 Bone, disease  
 Burn  
 Fertility  
 Hyperplasia  
 Hypertension  
 Intestine, disease  
 Muscle, disease  
 Rheumatoid arthritis  
 Skin, disease  
 Transplant rejection  
 Wound healing  
 (synthesis of cholestane compds. with a c17-alkyl side chain and an  
 aromatic A-ring for use in cell modulating therapy)

IT 57-88-5, Cholest-5-en-3-ol ( $3\beta$ )-, biological studies  
 RL: BSU (Biological study, unclassified); BIOL (Biological study)  
 (blood reduction; synthesis of cholestane compds. with a c17-alkyl side  
 chain and an aromatic A-ring for use in cell modulating therapy)

IT 9002-64-6, Parathyroid hormone  
 RL: BSU (Biological study, unclassified); BIOL (Biological study)  
 (suppression; synthesis of cholestane compds. with a c17-alkyl side  
 chain and an aromatic A-ring for use in cell modulating therapy)

IT 305812-17-3P 305812-18-4P 305812-52-6P  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological  
 study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU  
 (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT  
 (Reactant or reagent); USES (Uses)  
 (synthesis of cholestane compds. with a c17-alkyl side chain and an  
 aromatic A-ring for use in cell modulating therapy)

IT 305812-19-5P 305812-20-8P 305812-21-9P 305812-22-0P 305812-23-1P  
 305812-24-2P 305812-25-3P 305812-26-4P 305812-27-5P 305812-28-6P  
 305812-29-7P 305812-30-0P 305812-31-1P 305812-32-2P 305812-33-3P  
 305812-34-4P 305812-35-5P 305812-36-6P 305812-37-7P 305812-38-8P  
 305812-39-9P 305812-40-2P 305812-41-3P 305812-42-4P 305812-43-5P  
 305812-44-6P 305812-45-7P 305812-46-8P 305812-47-9P 305812-48-0P  
 305812-49-1P 305812-50-4P 305812-51-5P 305812-53-7P 305812-54-8P  
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 305812-60-6P 305812-61-7P 305812-62-8P 305812-63-9P 305812-64-0P  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological  
 study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use);  
 BIOL (Biological study); PREP (Preparation); USES (Uses)  
 (synthesis of cholestane compds. with a c17-alkyl side chain and an  
 aromatic A-ring for use in cell modulating therapy)

IT 74-88-4, Methyl iodide, reactions 75-03-6, Ethyl iodide 75-05-8,  
 Acetonitrile, reactions 78-77-3, Isobutyl bromide 96-33-3 98-88-4,  
 Benzoyl chloride 103-80-0, Phenylacetyl chloride 106-96-7, Propargyl  
 bromide 474-87-3 517-09-9 867-13-0 922-67-8, Methyl propiolate  
 1439-36-7, 1-Triphenylphosphoranylidene-2-propanone 3234-64-8,  
 1,1-Diethylpropargylamine 4736-60-1, Ethyl triphenylphosphonium iodide  
 7103-48-2, Estrone-3-tetrahydropyranyl ether 17963-41-6 305812-65-1  
 305812-66-2 305812-67-3 305812-69-5  
 RL: RCT (Reactant); RACT (Reactant or reagent)  
 (synthesis of cholestane compds. with a c17-alkyl side chain and an  
 aromatic A-ring for use in cell modulating therapy)

IT 229486-17-3P 305812-70-8P 305812-71-9P 305812-72-0P  
 305812-73-1P 305812-75-3P 305812-76-4P 305812-77-5P 305812-79-7P

provided by InfoChem.

STRUCTURE FILE UPDATES: 19 DEC 2003 HIGHEST RN 628722-21-4  
 DICTIONARY FILE UPDATES: 19 DEC 2003 HIGHEST RN 628722-21-4

TSCA INFORMATION NOW CURRENT THROUGH JULY 14, 2003

Please note that search-term pricing does apply when conducting SmartSELECT searches.

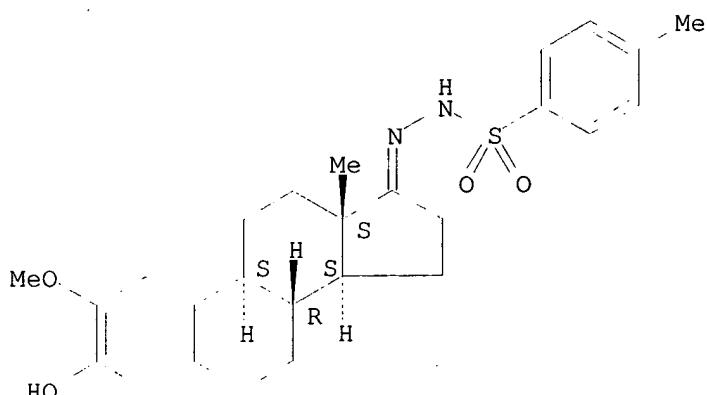
Crossover limits have been increased. See HELP CROSSOVER for details.

Experimental and calculated property data are now available. For more information enter HELP PROP at an arrow prompt in the file or refer to the file summary sheet on the web at:  
<http://www.cas.org/ONLINE/DBSS/registryss.html>

=> d ide can tot 176

L76 ANSWER 1 OF 12 REGISTRY COPYRIGHT 2003 ACS on STN  
 RN 438044-29-2 REGISTRY  
 CN Benzenesulfonic acid, 4-methyl-, (3-hydroxy-2-methoxyestra-1,3,5(10)-trien-17-ylidene)hydrazide (9CI) (CA INDEX NAME)  
 FS STEREOSEARCH  
 MF C26 H32 N2 O4 S  
 SR CA  
 LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL

Absolute stereochemistry.  
 Double bond geometry unknown.



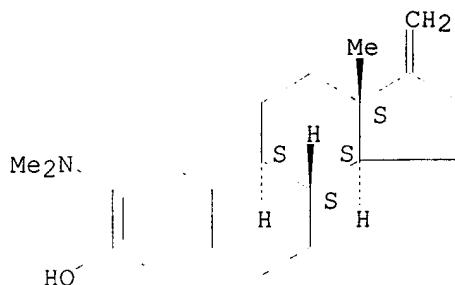
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 1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 137:47357

L76 ANSWER 2 OF 12 REGISTRY COPYRIGHT 2003 ACS on STN  
 RN 431901-97-2 REGISTRY  
 CN Estra-1,3,5(10)-trien-3-ol, 2-(dimethylamino)-17-methylene-, hydrochloride (9CI) (CA INDEX NAME)  
 FS STEREOSEARCH  
 MF C21 H29 N O . Cl H  
 SR CA  
 LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL

Absolute stereochemistry.



● HCl

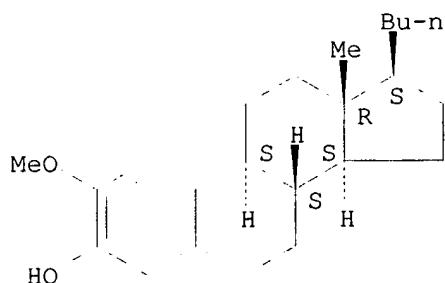
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2 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 137:47357

REFERENCE 2: 137:6309

L76 ANSWER 3 OF 12 REGISTRY COPYRIGHT 2003 ACS on STN  
 RN 431901-78-9 REGISTRY  
 CN 19,21-Dinorchola-1,3,5(10)-trien-3-ol, 2-methoxy- (9CI) (CA INDEX NAME)  
 FS STEREOSEARCH  
 MF C23 H34 O2  
 SR CA  
 LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL

Absolute stereochemistry.



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

3 REFERENCES IN FILE CA (1907 TO DATE)  
3 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 139:224972

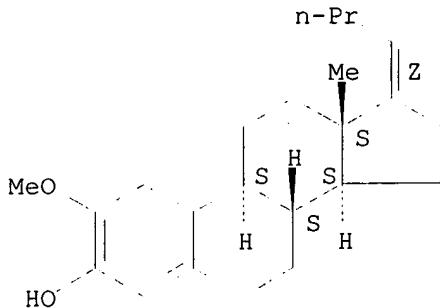
REFERENCE 2: 137:47357

REFERENCE 3: 137:6309

L76 ANSWER 4 OF 12 REGISTRY COPYRIGHT 2003 ACS on STN  
 RN 431901-77-8 REGISTRY  
 CN 19,21-Dinorchola-1,3,5(10),17(20)-tetraen-3-ol, 2-methoxy-, (17Z)- (9CI)

(CA INDEX NAME)  
 FS STEREOSEARCH  
 MF C23 H32 O2  
 SR CA  
 LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL

Absolute stereochemistry.  
 Double bond geometry as shown.



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

3 REFERENCES IN FILE CA (1907 TO DATE)  
 3 REFERENCES IN FILE CAPLUS (1907 TO DATE)

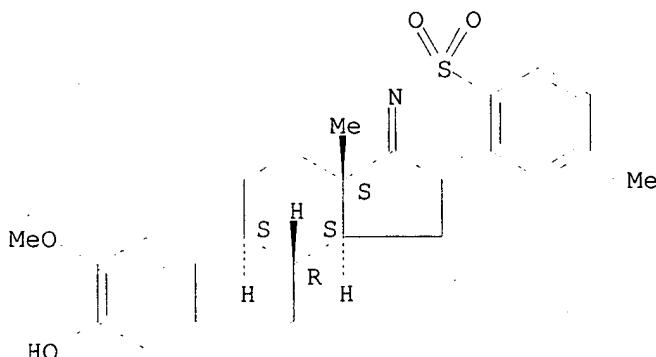
REFERENCE 1: 139:224972

REFERENCE 2: 137:47357

REFERENCE 3: 137:6309

L76 ANSWER 5 OF 12 REGISTRY COPYRIGHT 2003 ACS on STN  
 RN 431901-76-7 REGISTRY  
 CN Benzenesulfonamide, N-(3-hydroxy-2-methoxyestra-1,3,5(10)-trien-17-ylidene)-4-methyl- (9CI) (CA INDEX NAME)  
 FS STEREOSEARCH  
 MF C26 H31 N O4 S  
 SR CA  
 LC STN Files: CA, CAPLUS, TOXCENTER

Absolute stereochemistry.  
 Double bond geometry unknown.



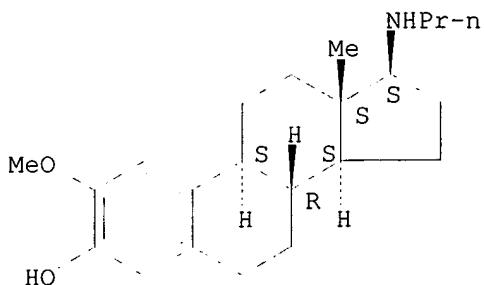
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1 REFERENCES IN FILE CA (1907 TO DATE)  
 1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 137:6309

L76 ANSWER 6 OF 12 REGISTRY COPYRIGHT 2003 ACS on STN  
 RN 431901-74-5 REGISTRY  
 CN Estra-1,3,5(10)-trien-3-ol, 2-methoxy-17-(propylamino)-, (17 $\beta$ )- (9CI)  
 (CA INDEX NAME)  
 FS STEREOSEARCH  
 MF C22 H33 N O2  
 SR CA  
 LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL

Absolute stereochemistry.



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

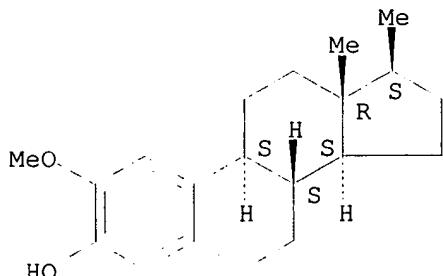
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 2 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 137:47357

REFERENCE 2: 137:6309

L76 ANSWER 7 OF 12 REGISTRY COPYRIGHT 2003 ACS on STN  
 RN 431901-71-2 REGISTRY  
 CN Estra-1,3,5(10)-trien-3-ol, 2-methoxy-17-methyl-, (17 $\beta$ )- (9CI) (CA  
 INDEX NAME)  
 FS STEREOSEARCH  
 MF C20 H28 O2  
 SR CA  
 LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL

Absolute stereochemistry.



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

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 3 REFERENCES IN FILE CAPLUS (1907 TO DATE)

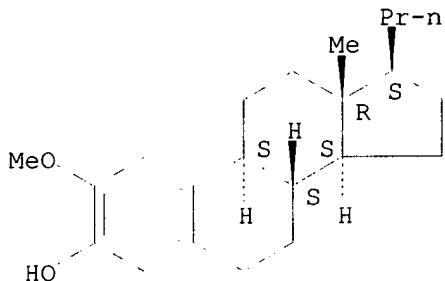
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REFERENCE 2: 137:47357

REFERENCE 3: 137:6309

L76 ANSWER 8 OF 12 REGISTRY COPYRIGHT 2003 ACS on STN  
 RN 431901-70-1 REGISTRY  
 CN Estra-1,3,5(10)-trien-3-ol, 2-methoxy-17-propyl-, (17 $\beta$ )- (9CI) (CA  
 INDEX NAME)  
 FS STEREOSEARCH  
 MF C22 H32 O2  
 SR CA  
 LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL

Absolute stereochemistry.



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

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 3 REFERENCES IN FILE CAPLUS (1907 TO DATE)

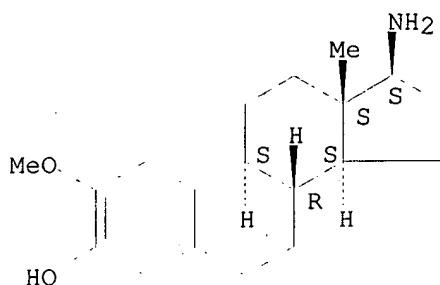
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REFERENCE 2: 137:47357

REFERENCE 3: 137:6309

L76 ANSWER 9 OF 12 REGISTRY COPYRIGHT 2003 ACS on STN  
 RN 431901-68-7 REGISTRY  
 CN Estra-1,3,5(10)-trien-3-ol, 17-amino-2-methoxy-, (17 $\beta$ )- (9CI) (CA  
 INDEX NAME)  
 FS STEREOSEARCH  
 MF C19 H27 N O2  
 SR CA  
 LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL

Absolute stereochemistry.



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

3 REFERENCES IN FILE CA (1907 TO DATE)  
3 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 139:224972

REFERENCE 2: 137:47357

REFERENCE 3: 137:6309

L76 ANSWER 10 OF 12 REGISTRY COPYRIGHT 2003 ACS on STN

RN 229486-18-4 REGISTRY

CN 19-Norpregna-1,3,5(10)-trien-3-ol, 2-methoxy- (9CI) (CA INDEX NAME)

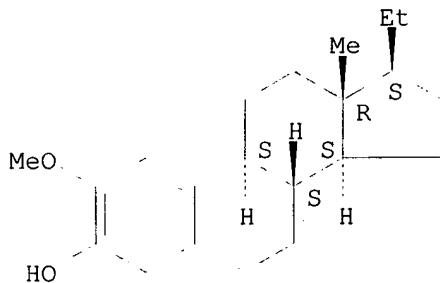
FS STEREOSEARCH

MF C21 H30 O2

SR CA

LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL

Absolute stereochemistry.



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

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4 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 139:224972

REFERENCE 2: 137:47357

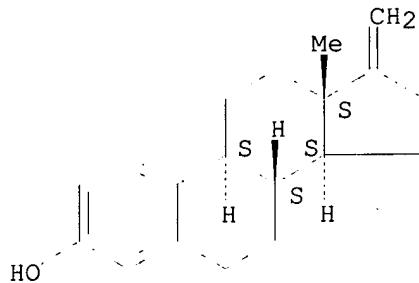
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REFERENCE 4: 131:88083

L76 ANSWER 11 OF 12 REGISTRY COPYRIGHT 2003 ACS on STN  
RN 34111-53-0 REGISTRY

CN Estra-1,3,5(10)-trien-3-ol, 17-methylene- (7CI, 8CI, 9CI) (CA INDEX NAME)  
 FS STEREOSEARCH  
 MF C19 H24 O  
 LC STN Files: BEILSTEIN\*, CA, CAOLD, CAPLUS, CASREACT, TOXCENTER, USPATFULL  
 (\*File contains numerically searchable property data)

Absolute stereochemistry.



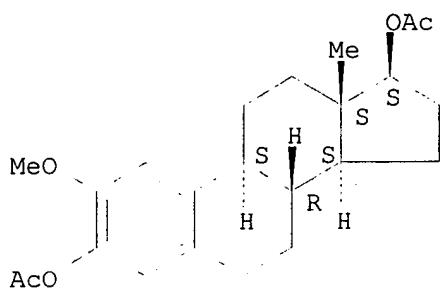
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 19 REFERENCES IN FILE CAPLUS (1907 TO DATE)  
 1 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

REFERENCE 1: 139:224972  
 REFERENCE 2: 138:348841  
 REFERENCE 3: 136:37829  
 REFERENCE 4: 133:208036  
 REFERENCE 5: 132:347795  
 REFERENCE 6: 132:308544  
 REFERENCE 7: 129:54482  
 REFERENCE 8: 128:294938  
 REFERENCE 9: 128:154277  
 REFERENCE 10: 127:293468

L76 ANSWER 12 OF 12 REGISTRY COPYRIGHT 2003 ACS on STN  
 RN 7291-57-8 REGISTRY  
 CN Estra-1,3,5(10)-triene-3,17-diol, 2-methoxy-, diacetate, (17 $\beta$ )- (9CI)  
 (CA INDEX NAME)  
 OTHER CA INDEX NAMES:  
 CN Estra-1,3,5(10)-triene-3,17 $\beta$ -diol, 2-methoxy-, diacetate (7CI, 8CI)  
 CN Estradiol, 2-methoxy-, diacetate (6CI)  
 FS STEREOSEARCH  
 MF C23 H30 O5  
 LC STN Files: BEILSTEIN\*, CA, CAOLD, CAPLUS, TOXCENTER, USPATFULL  
 (\*File contains numerically searchable property data)

Absolute stereochemistry.



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

11 REFERENCES IN FILE CA (1907 TO DATE)  
11 REFERENCES IN FILE CAPLUS (1907 TO DATE)  
3 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

REFERENCE 1: 139:369731

REFERENCE 2: 139:224972

REFERENCE 3: 137:47357

REFERENCE 4: 137:6309

REFERENCE 5: 134:295993

REFERENCE 6: 117:226505

REFERENCE 7: 90:121859

REFERENCE 8: 73:116788

REFERENCE 9: 72-121765

REFERENCE 10: 64:53436

=> d his 176-

I-76 (FILE 'REGISTRY' ENTERED AT 10:00:20 ON 21 DEC 2003)  
12 S I-73 I-75

FILE 'HCAOLD' ENTERED AT 10:10:31 ON 21 DEC 2003  
1.77 A S 1.76

FILE 'HCAPLUS' ENTERED AT 10:10:45 ON 21 DEC 2003  
L78 30 S L76  
L79 27 S L78 AND (PD<=20010208 OR PRD<=20010208 OR AD<=20010208)  
L80 3 S L78 AND L47-L60  
L81 29 S L63,L79-L80  
L82 2 S L78 NOT L81

FILE 'HCAOLD' ENTERED AT 10:12:46 ON 21 DEC 2003  
SEL AN L77  
EDIT /AN /OREF

FILE 'HCAPLUS' ENTERED AT 10:13:12 ON 21 DEC 2003  
L83 6 S E66-E69  
L84 5 S L83 NOT MAZUR ?/AU

L85            31 S L81,L84  
 L86            26 S L81 NOT L84

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=> fil hcaold  
 FILE 'HCAOLD' ENTERED AT 10:14:44 ON 21 DEC 2003  
 USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.  
 PLEASE SEE "HELP USAGETERMS" FOR DETAILS.  
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PRE-1967 CHEMICAL ABSTRACTS FILE WITH HOUR-BASED PRICING  
 FILE COVERS 1907-1966  
 FILE LAST UPDATED: 01 May 1997 (19970501/UP)

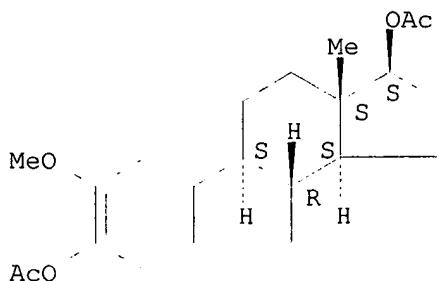
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L77 ANSWER 1 OF 4 HCAOLD COPYRIGHT 2003 ACS on STN  
 AN CA64:10030d CAOLD  
 TI thin-layer chromatography of estrogens on Kieselgel G  
 AU Lisboa, Belisario P.  
 IT        53-63-4     362-05-0     362-07-2     362-08-3     472-56-0     472-57-1  
         474-86-2     482-49-5     517-09-9     566-75-6     570-30-9     571-92-6  
         793-89-5     901-93-9     1035-77-4     1089-80-1     1150-90-9     1228-72-4  
         1228-73-5     1232-80-0     1247-70-7     1247-71-8     1474-52-8     1474-53-9  
         1476-34-2     1971-65-9     2208-12-0     2284-32-4     2464-15-5     3398-11-6  
         3434-79-5     3434-88-6     3563-27-7     3583-03-7     4551-97-7     5444-22-4  
         5976-62-5     6030-91-7     7004-98-0     7291-41-0     7291-47-6     7291-49-8  
         7291-51-2     7291-52-3     7291-53-4     7291-54-5     7291-56-7  
         7291-57-8     7323-86-6     7323-87-7     7323-90-2     7323-91-3  
         7323-92-4     7533-97-3     7684-84-6  
 IT        7291-57-8  
 RN        7291-57-8 HCAOLD  
 CN        Estra-1,3,5(10)-triene-3,17-diol, 2-methoxy-, diacetate, (17 $\beta$ )- (9CI)  
           (CA INDEX NAME)

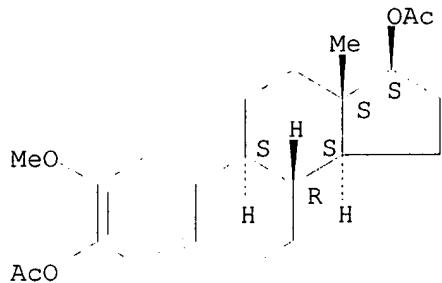
Absolute stereochemistry.



L77 ANSWER 2 OF 4 HCAOLD COPYRIGHT 2003 ACS on STN

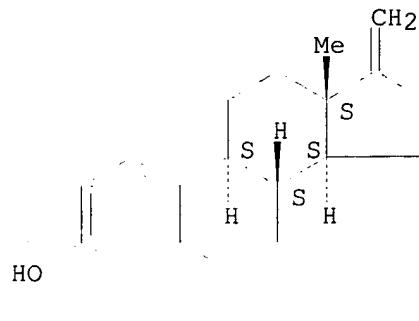
AN CA61:8583b CAOLD  
 TI use of double derivs. in the gas chromatography in urinary estrogens  
 AU Cox, R. I.; Bedford, A. R.  
 IT 2394-15-2 3434-85-3 5976-55-6 7291-57-8 18880-67-6  
 18880-86-9  
 IT 7291-57-8  
 RN 7291-57-8 HCAOLD  
 CN Estra-1,3,5(10)-triene-3,17-diol, 2-methoxy-, diacetate, (17 $\beta$ )- (9CI)  
 (CA INDEX NAME)

Absolute stereochemistry.



L77 ANSWER 3 OF 4 HCAOLD COPYRIGHT 2003 ACS on STN  
 AN CA56:515f CAOLD  
 TI distance effects in the steroid series - (II) influence of 17-substituents  
 on pK values of steroidal phenols  
 AU Legrand, Maurice; Delaroff, V.; Mathieu, J.  
 TI vegetable steroids-their utilization in the hemisynthesis of sexual  
 hormones and suprarenals  
 AU Grigot, Pierre  
 IT 53-63-4 1667-98-7 34111-53-0 35451-11-7 108041-85-6  
 IT 34111-53-0  
 RN 34111-53-0 HCAOLD  
 CN Estra-1,3,5(10)-trien-3-ol, 17-methylene- (7CI, 8CI, 9CI) (CA INDEX NAME)

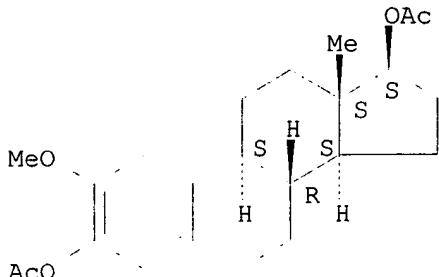
Absolute stereochemistry.



L77 ANSWER 4 OF 4 HCAOLD COPYRIGHT 2003 ACS on STN  
 AN CA52:13765i CAOLD  
 TI synthesis of 2-methoxyestrogens  
 AU Fishman, Jack  
 IT 362-07-2 362-08-3 7291-57-8 38781-50-9 52717-98-3  
 65932-49-2 65932-50-5 65932-51-6 65932-52-7 65932-53-8 84509-93-3  
 103278-44-0 120024-00-2  
 IT 7291-57-8  
 RN 7291-57-8 HCAOLD  
 CN Estra-1,3,5(10)-triene-3,17-diol, 2-methoxy-, diacetate, (17 $\beta$ )- (9CI)

(CA INDEX NAME)

Absolute stereochemistry.



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FILE LAST UPDATED: 19 Dec 2003 (20031219/ED)

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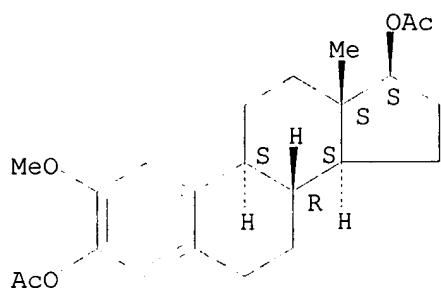
L88 ANSWER 1 OF 5 HCAPLUS COPYRIGHT 2003 ACS on STN  
AN 1966:53436 HCAPLUS  
DN 64:53436  
OREF 64:10030c-d  
ED Entered STN: 22 Apr 2001  
TI Thin-layer chromatography of estrogens on Kieselgel G.  
AU Lisboa, B. P.  
CS Karolinska Sjukhuset, Stockholm  
SO Clinica Chimica Acta (1966), 13(2), 179-99  
CODEN: CCATAR; ISSN: 0009-8981  
DT Journal  
LA German  
CC 58 (Hormones)  
AB A method for the separation and characterization of 51 steroid estrogens by ascending chromatography on silica gel G after single and multiple chromatography is presented. The steroids are characterized by their Rf-values in several systems, color reactions, and derivative formation. The possibility of separating steroids of similar polarity by thin-layer chromatography is discussed here, and compared with the results obtained

by other anal. procedures. Also, the correlation between steroid structure and mobility is discussed.

- IT Estrogenic hormones or principles  
 (chromatography of)
- IT 16,17-Secoaestra-1,3,5(10)-trien-17-oic acid, 3 $\beta$ -hydroxy-Estra-1,3,5(10)-triene-16 $\alpha$ ,17 $\beta$ -diol, 3-methoxy-Estra-1,3,5(10-trien-17-one, 3,15 $\alpha$ -dihydroxy-Estra-1,3,6(10)-triene-3,16 $\alpha$ ,17 $\beta$ -triol, 2-methoxy-(chromatography of)
- IT 50-27-1, Estriol 50-28-2, Estradiol 53-16-7, Estrone 53-63-4, Estra-1,3,5(10)-triene-3-ol 57-91-0, 17 $\alpha$ -Estradiol 362-05-0, Estra-1,3,5(10)-triene-2,3,17 $\beta$ -triol 362-08-3, Estra-1,3,5(10-trien-17-one, 3-hydroxy-2-methoxy- 472-56-0, Estra-1,3,5(10)-triene-3-ol, 16 $\alpha$ ,17 $\alpha$ -epoxy- 472-57-1, Estra-1,3,5(10)-triene-3-ol, 16 $\beta$ ,17 $\beta$ -epoxy- 474-86-2, Equilin 482-49-5, Doisynolic acid 517-09-9, Equilenin 547-81-9, Estra-1,3,5(10)-triene-3,16 $\beta$ ,17 $\beta$ -triol 566-75-6, Estra-1,3,5(10)-triene-16-one, 3,17 $\beta$ -dihydroxy- 566-76-7, Estra-1,3,5(10-trien-17-one, 3,16 $\alpha$ -dihydroxy- 570-30-9, Estra-1,3,5(10)-triene-3,15 $\alpha$ ,17 $\beta$ -triol 571-92-6, Estra-1,3,5(10)-triene-6-one, 3,17 $\beta$ -dihydroxy- 793-89-5, Estra-1,3,5(10)-triene-3,16 $\beta$ ,17 $\alpha$ -triol 901-93-9, Estrone, acetate 966-06-3, Estra-1,3,5(10-trien-17-one, 3,16 $\beta$ -dihydroxy- 1035-77-4, Estra-1,3,5(10)-triene-17 $\beta$ -ol, 3-methoxy- 1089-80-1, Estra-1,3,5(10),9(11)-tetraen-17-one, 3-hydroxy- 1150-90-9, Estra-1,3,5(10),16-tetraen-3-ol 1228-72-4, Estra-1,3,5(10)-triene-3,16 $\alpha$ ,17 $\alpha$ -triol 1228-73-5, Estra-1,3,5(10)-triene-16,17-dione, 3-hydroxy- 1229-24-9, Estra-1,3,5(10)-triene-3,6 $\alpha$ ,17 $\beta$ -triol 1229-25-0, Estra-1,3,5(10-trien-17-one, 3,6 $\beta$ -dihydroxy- 1232-80-0, Estra-1,3,5(10)-triene-2,3,16 $\alpha$ ,17 $\beta$ -tetrol 1247-70-7, Estra-1,3,5(10-trien-17-one, 3,16 $\beta$ -dihydroxy-, diacetate 1247-71-8, Estra-1,3,5(10-trien-17-one, 3,16 $\alpha$ -dihydroxy-, diacetate 1474-52-8, 17 $\alpha$ -Estradiol, diacetate 1476-78-4, Estra-1,3,5(10-trien-17-one, 3,6 $\alpha$ -dihydroxy- 1971-65-9, Estra-1,3,5(10),6-tetraene-3,17 $\beta$ -diol, diacetate 2208-12-0, Estra-1,3,5(10),6-tetraen-17-one, 3-hydroxy- 2284-32-4, Estriol, triacetate 2487-47-0, Estra-1,3,5(10-trien-17-one, 3,7 $\beta$ -dihydroxy- 2487-49-2, Estra-1,3,5(10-trien-17-one, 3,7 $\alpha$ -dihydroxy- 3131-23-5, Estra-1,3,5(10-trien-17-one, 3,4-dihydroxy- 3398-11-6, Estra-1,3,5(10)-triene-3,7 $\alpha$ ,17 $\beta$ -triol 3434-79-5, Estra-1,3,5(10)-triene-16 $\beta$ ,17 $\beta$ -diol, 3-methoxy- 3434-88-6, Estradiol, diacetate 3563-27-7, Estra-1,3,5(10),7-tetraene-3,17 $\beta$ -diol 3583-03-7, Estra-1,3,5(10)-triene-3,6 $\beta$ ,17 $\beta$ -triol 4551-97-7, Estra-1,3,5(10)-triene-6 $\beta$ ,17 $\beta$ -diol, 3-methoxy- 5210-15-1, Estra-1,3,5(10-trien-17-one, 3,11 $\alpha$ -dihydroxy- 5444-22-4, Estra-1,3,5(10)-triene-3,11 $\beta$ ,17 $\beta$ -triol 5976-62-5, Estra-1,3,5(10-trien-17-one, 4-hydroxy-3-methoxy- 6030-91-7, Equilenin, acetate 6803-21-0, Estra-1,3,5(10-trien-17-one, 3,11 $\beta$ -dihydroxy- 7004-98-0, Estra-1,3,5(10)-triene-16 $\alpha$ ,17 $\alpha$ -diol, 3-methoxy- 7291-41-0, Estra-1,3,5(10),6-tetraene-3,17 $\beta$ -diol 7291-47-6, Estra-1,3,5(10)-triene-6 $\alpha$ ,17 $\beta$ -diol, 3-methoxy- 7291-49-8, Estra-1,3,5(10)-triene-3,6 $\alpha$ ,16 $\alpha$ ,17 $\beta$ -tetrol 7291-51-2, Estra-1,3,5(10),6-tetraen-3-ol, acetate 7291-52-3, Estra-1,3,5(10),9(11)-tetraen-17-one, 3-hydroxy-, acetate 7291-53-4, Estra-1,3,5(10)-triene-11,17-dione, 3-hydroxy-, acetate 7291-54-5, Estra-1,3,5(10)-triene-16,17-dione, 3-hydroxy-, acetate 7291-56-7, Estra-1,3,5(10)-triene-2,3,17 $\beta$ -triol, triacetate 7291-57-8, Estra-1,3,5(10)-triene-3,17 $\beta$ -diol, 2-methoxy-, diacetate 7323-86-6, Estra-1,3,5(10)-triene-6-one, 3,16 $\alpha$ ,17 $\beta$ -trihydroxy- 7323-87-7, Estra-1,3,5(10)-triene-3,6,7,17 $\beta$ -tetrol 7323-90-2, Estra-1,3,5(10-trien-17-one, 3,6 $\beta$ -dihydroxy-, diacetate 7323-91-3, Estra-1,3,5(10)-triene-3,17 $\beta$ -diol, 6 $\beta$ ,7 $\beta$ -epoxy-, diacetate 7323-92-4, Estra-1,3,5(10)-triene-3,6 $\alpha$ ,7 $\beta$ ,17 $\beta$ -tetrol, tetraacetate 7533-97-3, Estra-1,3,5(10)-triene-11,17-dione, 3-hydroxy- 7684-84-6,

Estra-1,3,5(10)-triene-7,17-dione, 3-hydroxy-, acetate 109784-48-7,  
 2-Phenanthrenecarboxylic acid, 1-ethyl-1,2,3,4,4a,9,10,10a-octahydro-7-  
 hydroxy-2-methyl-  
 (chromatography of)  
 IT 362-07-2, Estra-1,3,5(10)-triene-3,17 $\beta$ -diol, 2-methoxy- 1476-34-2,  
 Estra-1,3,5(10)-triene-6,17-dione, 3-hydroxy- 2464-15-5,  
 Estra-1,3,5(10)-triene-7,17-dione, 3-hydroxy- 3398-12-7,  
 Estra-1,3,5(10)-trien-7-one, 3,17 $\beta$ -dihydroxy-  
 (preparation of)  
 IT 7291-57-8, Estra-1,3,5(10)-triene-3,17 $\beta$ -diol, 2-methoxy-,  
 diacetate  
 (chromatography of)  
 RN 7291-57-8 HCPLUS  
 CN Estra-1,3,5(10)-triene-3,17-diol, 2-methoxy-, diacetate, (17 $\beta$ )- (9CI)  
 (CA INDEX NAME)

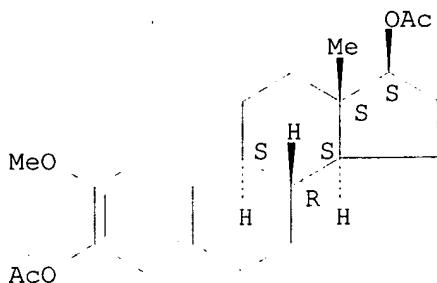
Absolute stereochemistry.



L88 ANSWER 2 OF 5 HCPLUS COPYRIGHT 2003 ACS on STN  
 AN 1964:449185 HCPLUS  
 DN 61:49185  
 OREF 61:8583a-c  
 ED Entered STN: 22 Apr 2001  
 TI The use of double derivatives in the gas chromatography of urinary  
 estrogens  
 AU Cox, R. I.; Bedford, A. R.  
 CS Univ. Adelaide  
 SO Steroids (1964), 3(6), 663-9  
 CODEN: STEDAM; ISSN: 0039-128X  
 DT Journal  
 LA Unavailable  
 CC 58 (Hormones)  
 AB Double derivs. of urinary estrogens, either 3-Me ether acetates or 3-Me  
 ether trimethylsilyl ethers, were prep'd, and suitable conditions for their  
 chromatography investigated. Second- and 3rd-trimester pregnancy urine  
 exts. showed well defined sym. peaks at characteristic retention times for  
 derivs. of the 3 major estrogens (estrone, estradiol, and estriol) on the  
 gas chromatograph recordings. Background interference was more evident in  
 the 1st-trimester pregnancy urine but recordings were satisfactory where  
 concns. of 30-50  $\mu$ /24 hrs. were present. Since double derivs. may  
 be prepared as readily as single ones, the extra chemical purification obtained  
 in their preparation before gas chromatography is an advantage in detection and  
 estimation of these compds. in biol. samples.  
 IT Urine  
 (analysis, separation of estrogens)  
 IT Estra-1,3,5(10)-triene, 3-methoxy-16 $\alpha$ ,17 $\beta$ -bis(trimethylsiloxy)-  
 Estra-1,3,5(10)-triene, 3-methoxy-17 $\beta$ -(trimethylsiloxy)-  
 Estra-1,3,5(10)-triene-16 $\alpha$ ,17 $\beta$ -diol, 3-methoxy-, diacetate  
 (gas chromatography of)  
 IT 18880-67-6, Silane, [(3-methoxyestra-1,3,5(10)-trien-17 $\beta$ -

yl)oxy]trimethyl- 18880-86-9, Silane, [(3-methoxyestra-1,3,5(10)-trien-16 $\alpha$ ,17 $\beta$ -ylene)dioxy]bis[trimethyl-  
(chromatography (gas) of)  
IT 53-06-5, Cortisone 1624-62-0, Estra-1,3,5(10-trien-17-one, 3-methoxy-  
5976-55-6, Estra-1,3,5(10)-trien-17 $\beta$ -ol, 3-methoxy-, acetate  
7291-57-8, Estra-1,3,5(10)-triene-3,17 $\beta$ -diol, 2-methoxy-,  
diacetate  
(chromatography of)  
IT 7291-57-8, Estra-1,3,5(10)-triene-3,17 $\beta$ -diol, 2-methoxy-,  
diacetate  
(chromatography of)  
RN 7291-57-8 HCAPLUS  
CN Estra-1,3,5(10)-triene-3,17-diol, 2-methoxy-, diacetate, (17 $\beta$ )- (9CI)  
(CA INDEX NAME)

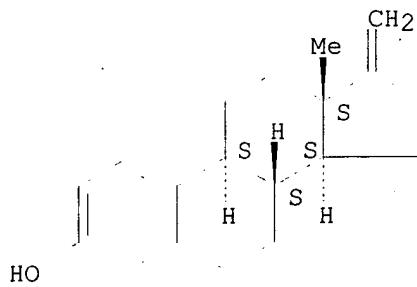
Absolute stereochemistry.



L88 ANSWER 3 OF 5 HCAPLUS COPYRIGHT 2003 ACS on STN  
AN 1962:2540 HCAPLUS  
DN 56:2540  
OREF 56:515f-g  
ED Entered STN: 22 Apr 2001  
TI Distance effects in the steroid series. II. Influence of 17-substituents  
on pK values of steroidal phenols  
AU Legrand, Maurice; Delaroff, Vladimir; Mathieu, Jean  
CS Roussel Uclaf, Paris  
SO Bulletin de la Societe Chimique de France (1961) 1346-8  
CODEN: BSCFAS; ISSN: 0037-8968  
DT Journal  
LA Unavailable  
CC 36 (Steroids)  
AB The pK values for steroidal phenols were found to vary with the type of  
substitution in the D-ring. Measurements were made spectrophotometrically  
in MeOH-MeONa and Na2B4O7.10H2O-Na2CO3 solns. at concns. of 2 +  
10-4M and the values reported as pK-pK 17 $\beta$ -estradiol as follows:  
estra-1,3,5(10)-trien-3-ol (-0.01, 0.00); 17 $\alpha$ -estradiol (-0.03,  
0.00); D-homo-17 $\alpha$  $\beta$ -estradiol (0.00, 0.01); 17-methyleneestra-  
1,3,5(10)-trien-3-ol (-0.02, -0.05); 17 $\beta$ -acetylestera-1,3,5(10)-trien-  
3-ol (-0.07, -0.06); D-homoestrone (-0.09, -0.10); estrone (-0.10,  
-0.10). The small differences were found to be statistically significant.  
IT Steroids  
(distant group effect on)  
IT Steroids  
(natural sources of)  
IT Substituents  
(neighboring, ionization (pK) of steroidal phenols in relation to)  
IT Ionization  
(of steroidal phenols, neighboring group effect on)  
IT D-Homoestra-1,3,5(10)-trien-17-one, 3-hydroxy-  
(ionization of)

IT 53-16-7, Estrone 53-63-4, Estra-1,3,5(10)-trien-3-ol 57-91-0,  
 17 $\alpha$ -Estradiol 1667-98-7, 19-Norpregna-1,3,5(10)-trien-20-one,  
 3-hydroxy- 34111-53-0, Estra-1,3,5(10)-trien-3-ol, 17-methylene-  
 35451-11-7, D-Homoestra-1,3,5(10)-triene-3,17 $\beta$ -diol  
 (ionization of)  
 IT 34111-53-0, Estra-1,3,5(10)-trien-3-ol, 17-methylene-  
 (ionization of)  
 RN 34111-53-0 HCAPLUS  
 CN Estra-1,3,5(10)-trien-3-ol, 17-methylene- (7CI, 8CI, 9CI) (CA INDEX NAME)

Absolute stereochemistry.



L88 ANSWER 4 OF 5 HCAPLUS COPYRIGHT 2003 ACS on STN  
 AN 1962:2539 HCAPLUS  
 DN 56:2539  
 OREF 56:515f  
 ED Entered STN: 22 Apr 2001  
 TI Vegetable steroids. Their utilization in the hemisynthesis of sexual hormones and suprarenals  
 AU Grigot, Pierre  
 SO Prods. Pharm. (1961), 16, 379-401  
 DT Journal  
 LA Unavailable  
 CC 36 (Steroids)  
 AB A review with 78 references.  
 IT Steroids  
 (distant group effect on)  
 IT Steroids  
 (natural sources of)

L88 ANSWER 5 OF 5 HCAPLUS COPYRIGHT 2003 ACS on STN  
 AN 1958:77293 HCAPLUS  
 DN 52:77293  
 OREF 52:13765i,13766a-h  
 ED Entered STN: 22 Apr 2001  
 TI Synthesis of 2-methoxyestrogens  
 AU Fishman, Jack  
 CS Sloan-Kettering Inst. for Cancer Research, New York, NY  
 SO Journal of the American Chemical Society (1958), 80, 1213-16  
 CODEN: JACSAT; ISSN: 0002-7863  
 DT Journal  
 LA Unavailable  
 CC 10 (Organic Chemistry)  
 OS CASREACT 52:77293  
 AB Estrone (I) (1.71 g.) added to 0.210 g. KOH in 50 cc. absolute EtOH, warmed, treated with 0.853 g. 2,5-C1(O2N)C6H3Bz (II), refluxed 24 hrs., concentrated to half the original volume, cooled, poured into N NaOH, extracted with CHCl3, and the extract evaporated yielded 1.365 g. 3-(2-benzoyl-4-nitrophenyl) ether (III) of I, m. 240-3° (MeOH), [math]\alpha26D 88°; the aqueous alkaline solution acidified gave 0.7 g. unchanged I. III (100 mg.) in 0.5 cc. cold. concentrated

H<sub>2</sub>SO<sub>4</sub> treated after 0.5 hr. with 4 cc. glacial AcOH then with 0.5 cc. 30% H<sub>2</sub>O<sub>2</sub>, allowed to stand 0.5 hr., poured into iced H<sub>2</sub>O, filtered, the solid washed with H<sub>2</sub>O, treated with excess CH<sub>2</sub>N<sub>2</sub> in Et<sub>2</sub>O, the resulting needles, m. 144-7°, refluxed 1 hr. with piperidine, diluted with C<sub>6</sub>H<sub>6</sub>, washed with dilute H<sub>2</sub>SO<sub>4</sub>, the C<sub>6</sub>H<sub>6</sub> layer extracted with dilute aqueous NaOH, and the aqueous extract

acidified and extracted with CHCl<sub>3</sub> gave a few crystals of the 13,17-secolactone, m. 204-7°. 17β-Estradiol (IV) (5 g.) and 0.586 g. KOH in 100 cc. EtOH refluxed 48 hrs. with 2.4 g. II, concentrated to half the original volume, poured into 200 cc. N NaOH, extracted with CHCl<sub>3</sub>, the extract dried, evaporated, and the residual viscous oil dissolved in 50 cc. 1:1 petr. ether-C<sub>6</sub>H<sub>6</sub> and chromatographed on 150 g. Al<sub>2</sub>O<sub>3</sub> gave 90 mg. II, m. 114-16°, and 4.12 g. 3,17β-dihydroxy-1,3,5-(10)-estratriene 3-(2-benzoyl-4-nitrophenyl) ether (V), m. 97-105°, [α]26D 40°. V was oxidized in excellent yield to III. Further elution of the column with Et<sub>2</sub>O gave some unreacted IV. V with Ac<sub>2</sub>O and pyridine gave the acetate (VI) of V, viscous oil. VI (7.5 g.) in 4 cc. glacial AcOH treated slowly with cooling and shaking with 10 cc. cold concentrated H<sub>2</sub>SO<sub>4</sub>, kept 0.5 hr. at room temperature, diluted with 40 cc. glacial AcOH, treated.

dropwise with 10 cc. 1:1 AcOH-30% H<sub>2</sub>O<sub>2</sub>, kept 0.5 hr. at room temperature, poured

into iced H<sub>2</sub>O, and filtered gave 4.6 g. 2-OH derivative (VII) of VI, m. 170-2° (MeOH), [α]28.8D 21.0°; 2nd crop, 1.6 g. VII (2.2 g.) in 50 cc. EtOH kept 24 hrs. at 5° with excess CH<sub>2</sub>N<sub>2</sub> in Et<sub>2</sub>O and evaporated gave 2 g. 2-MeO analog (VIII) of VII, m. 169-71°, [α]26D 36°. VIII (432 mg.) refluxed 1 hr. in 20 cc. pyridine, diluted with 100 cc. C<sub>6</sub>H<sub>6</sub>, washed with dilute H<sub>2</sub>SO<sub>4</sub> and N NaOH, evaporated, and the oily residue (446 mg.) chromatographed on 16 g. Al<sub>2</sub>O<sub>3</sub> yielded 180 mg. 2-methoxy-3-hydroxy-17β-acetoxy-1,3,5(10)-estratriene (IX), plates changing to needles, m. 194-6° (C<sub>6</sub>H<sub>6</sub>-petr. ether), [α]26D 125°. IX hydrolyzed under N with 5% alc. KOH gave 2-methoxy-17β-estradiol (X), m. 184-6° (C<sub>6</sub>H<sub>6</sub>). VIII (1.43 g.) in 50 cc. 6% alc. KOH refluxed 2 hrs. under N, diluted with H<sub>2</sub>O, and extracted with C<sub>6</sub>H<sub>6</sub> gave 700 mg. X, blades, m. 188-90° (Me<sub>2</sub>CO), [α]21D 100°; diacetate of X, needles, m. 165-6° (MeOH), [α]26.5D 53°. X partially dissolved in N NaOH and shaken with excess BzCl gave 3-monobenzoate (XI) of X, m. 195-8° (MeOH), [α]28D 72°. VIII (203 mg.) in 40 cc. EtOH containing 8 cc. concentrated H<sub>2</sub>SO<sub>4</sub> refluxed 24 hrs., diluted with H<sub>2</sub>O, extracted with Et<sub>2</sub>O,

and the

extract worked up gave 180 mg. 2-MeO derivative (XII) of V, m. 125-6° (MeOH), [α]28D 61°, also obtained in considerably lower yield by alkaline hydrolysis of VIII at room temperature XII (290 mg.) in 40 cc. Me<sub>2</sub>CO

treated dropwise with 8N CrO<sub>3</sub>-H<sub>2</sub>SO<sub>4</sub> until an orange-brown color persisted, kept 15 min. at room temperature, poured into H<sub>2</sub>O, and extracted with CHCl<sub>3</sub> yielded

231 mg. 2-MeO derivative (XIII) of I, needles, m. 204-5° (MeOH), [α]28D 89°. XIII (240 mg.) in 20 cc. piperidine refluxed 1 hr., cooled, diluted with 100 cc. C<sub>6</sub>H<sub>6</sub>, washed with dilute H<sub>2</sub>SO<sub>4</sub>, dried, evaporated, the residual oil subjected to a 99-transfer countercurrent distribution between 70% aqueous MeOH and CCl<sub>4</sub>, and the combined tubes 14-32 filtered through Al<sub>2</sub>O<sub>3</sub> and crystallized from aqueous MeOH gave 108 mg. 2-methoxyestrone, blades, m. 188-91°, giving with NaOH and BzCl the 3-monobenzoate, needles, m. 225-8°, which was also obtained by oxidation of XI with CrO<sub>3</sub>.

IT Estra-1,3,5(10)-trien-17β-ol, 3-(2-benzoyl-4-nitrophenoxy)- Estra-1,3,5(10)-trien-17β-ol, 3-(2-benzoyl-4-nitrophenoxy)-, acetate Estra-1,3,5(10)-trien-17β-ol, 3-(2-benzoyl-4-nitrophenoxy)-2-methoxy- Estra-1,3,5(10)-trien-17β-ol, 3-(2-benzoyl-4-nitrophenoxy)-2-methoxy-, acetate

IT 362-07-2, Estradiol, 2-methoxy-

(and derivs.)  
IT 362-08-3, Estrone, 2-methoxy- 38781-50-9, Benzophenone,  
2-(2,17 $\beta$ -dihydroxyestra-1,3,5(10)-trien-3-yloxy)-5-nitro-, 17-acetate  
65932-49-2, Benzophenone, 2-(17 $\beta$ -hydroxyestra-1,3,5(10)-trien-3-  
yloxy)-5-nitro- 65932-50-5, Benzophenone, 2-(17 $\beta$ -hydroxyestra-  
1,3,5(10)-trien-3-yloxy)-5-nitro-, acetate 65932-51-6, Benzophenone,  
2-(17 $\beta$ -hydroxy-2-methoxyestra-1,3,5(10)-trien-3-yloxy)-5-nitro-,  
acetate 65932-52-7, Benzophenone, 2-(17 $\beta$ -hydroxy-2-methoxyestra-  
1,3,5(10)-trien-3-yloxy)-5-nitro- 65932-53-8, Estra-1,3,5(10)-trien-17-  
one, 3-(2-benzoyl-4-nitrophenoxy)-2-methoxy- 103278-44-0,  
Estra-1,3,5(10)-trien-17-one, 3-(2-benzoyl-4-nitrophenoxy)- 120024-00-2,  
Estrone, 2-methoxy-, benzoate  
(preparation of)

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L89 ANSWER 1 OF 22 HCAPLUS COPYRIGHT 2003 ACS on STN  
AN 2001:916405 HCAPLUS  
DN 136:37829  
ED Entered STN: 20 Dec 2001  
TI Steroids as neurochemical stimulators of the VNO to alleviate pain  
IN Berliner, David L.; Monti-Bloch, Luis  
PA Pherin Pharmaceuticals, Inc., USA  
SO U.S., 286 pp., Cont.-in-part of U.S. Ser. No. 725,862, abandoned.  
CODEN: USXXAM  
DT Patent  
LA English  
IC ICM A61K031-56  
NCL 514177000  
CC 32-6 (Steroids)  
Section cross-reference(s): 1, 2, 63

FAN.CNT 12

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 6331534	B1	20011218	US 1997-919621	19970828 <--
	US 5563131	A	19961008	US 1994-286073	19940804 <--
	US 6066627	A	20000523	US 1996-625268	19960329 <--
	US 6057439	A	20000502	US 1996-686092	19960723 <--
PRAI	US 1994-286073	A2	19940804 <--		
	US 1996-625268	A2	19960329 <--		
	US 1996-686092	A2	19960723 <--		
	US 1996-725862	B2	19961004 <--		

OS MARPAT 136:37829

AB Steroids such as formula I [R1 = oxo, (substituted)OH; R2 = (substituted)alkyl; R3 = H, oxo, halo, (substituted)OH; R4-R12 = independently H, halo, (halo-substituted)methyl; R2R3 may = cyclic ether; R13 = H, Me, methylene, etc.] are prepared. Thus, 3 $\alpha$ - and 3 $\beta$ -pregna-4,20-dien-3-ols were prepared in 14 and 23% yields, resp., by reduction of pregn-4,20-dien-3-one using lithium trisiamylborohydride in dry THF. The invention relates to a method of alleviating pain. The method comprises nasally administering a steroid which is a human vomeropherin, such that the vomeropherin binds to a specific neuroepithelial receptor. The steroid or steroids is/are preferably administered in the form of a pharmaceutical composition containing one or more pharmaceutically acceptable carriers. Autonomic responses to stimulation of the vomeronasal organ (VNO) by the prepared compds. was measured.

ST steroid prepn neurochem stimulator vomeronasal organ pain

IT Drug delivery systems

(nasal; steroids as neurochem. stimulators of the VNO to alleviate pain)

IT Neurohormone receptors

RL: BSU (Biological study, unclassified); BIOL (Biological study)

(neuroepithelial; steroids as neurochem. stimulators of the VNO to alleviate pain)

- IT Pain  
 (steroids as neurochem. stimulators of the VNO to alleviate pain)
- IT Steroids, preparation  
 RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)  
 (steroids as neurochem. stimulators of the VNO to alleviate pain)
- IT Nose  
 (vomeronasal organ; steroids as neurochem. stimulators of the VNO to alleviate pain)
- IT 846-45-7P 1150-90-9P, Estra-1,3,5(10),16-tetraen-3-ol 1224-94-8P  
 2118-31-2P 4075-07-4P, Androsta-4,16-dien-3-one 28336-31-4P  
 30505-67-0P **34111-53-0P** 35456-72-5P 65754-63-4P,  
 Pregna-1,4,20-trien-3-one 71496-98-5P, Estra-4,16-dien-3-one  
 77257-06-8P 86306-95-8P 99898-93-8P 161061-70-7P 161061-73-0P  
 161061-86-5P 161061-93-4P 161061-95-6P 161061-97-8P 161061-98-9P,  
 Estra-5(10),16-dien-3-one 161062-00-6P 177349-45-0P 177349-47-2P  
 177349-58-5P, 24-Norchola-4,22-dien-3-one 177349-64-3P 177349-66-5P  
 177349-74-5P 177794-25-1P 177794-29-5P 177794-30-8P 177856-06-3P  
 177856-07-4P, Estra-1,3,5(10),6,16-pentaen-3-ol 177856-09-6P  
 177856-10-9P, Estra-1,3,5(10),7,16-pentaen-3-ol 177856-12-1P  
 177856-13-2P, Estra-1,3,5,7,9,16-hexaen-3-ol 177856-15-4P 177856-17-6P  
 177856-20-1P 178688-50-1P 186183-19-7P, 19-Norpregna-5(10),20-dien-3-one  
 186183-23-3P 186183-25-5P 200511-32-6P 200511-37-1P  
 200511-39-3P 205994-17-8P 205994-18-9P 205994-19-0P 379738-50-8P  
 RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)  
 (steroids as neurochem. stimulators of the VNO to alleviate pain)
- IT 53-63-4P, Estra-1,3,5(10)-trien-3-ol 472-56-0P 1232-18-4P,  
 Pregn-4-en-3-one 2862-58-0P 2872-90-4P, Androst-4-en-3-one  
 23062-06-8P 26400-72-6P 35581-65-8P, Pregna-4,16-dien-3-one  
 58594-49-3P 63014-91-5P, Androsta-4,6,16-trien-3-one 86306-63-0P  
 86306-96-9P 99898-92-7P, 19-Norpregna-1,3,5(10)-trien-20-yn-3-ol  
 114611-55-1P, Androsta-4,16-diene-3,6-dione 161061-71-8P 161061-72-9P  
 161061-77-4P 161061-81-0P 161061-82-1P 161061-83-2P 161061-84-3P  
 161061-99-0P, Estra-4,9,16-trien-3-one 161062-01-7P 161062-02-8P  
 161062-04-0P, Estra-1,3,5(10),7-tetraen-3-ol 161062-05-1P  
 161062-06-2P, Estra-1,3,5(10),6-tetraen-3-ol 161062-08-4P 161062-09-5P  
 177349-46-1P 177349-48-3P, 24-Norchola-4,20(22)-dien-3,6-dione  
 177349-49-4P, 24-Norchola-4,20(22)-dien-3-one 177349-54-1P  
 177349-55-2P 177349-56-3P, Pregna-4,16-diene-3,6-dione 177349-57-4P,  
 Pregna-4,17(20),20-triene-3,6-dione 177349-59-6P 177349-60-9P,  
 24-Norchola-4,22-diene-3,6-dione 177349-61-0P 177349-63-2P  
 177349-65-4P 177349-67-6P 177349-68-7P 177349-69-8P 177349-72-3P,  
 Pregna-1,4,20-trien-3-ol 177349-73-4P, Pregna-4,20-diene-3,6-dione  
 177695-29-3P 177794-21-7P 177794-22-8P 177794-23-9P 177794-24-0P  
 177794-26-2P 177794-27-3P 177794-31-9P 177794-32-0P 177856-05-2P  
 177856-08-5P 177856-11-0P 177856-14-3P 177856-16-5P 177856-21-2P  
 177856-22-3P 177856-23-4P 178033-52-8P, Estra-1,3,5(10),16-tetraene-3,6-diol  
 186183-17-5P 186183-18-6P 186183-20-0P,  
 19-Norpregna-5(10),20-dien-3-ol 186183-21-1P 186183-22-2P,  
 19-Norpregna-4,9,20-trien-3-one 186183-24-4P 186183-26-6P  
 197094-33-0P 197094-34-1P 200574-68-1P, 19,21-Dinorchol-4-en-3-one  
 202718-04-5P 205994-20-3P 205994-21-4P 205994-22-5P 205994-23-6P  
 250683-26-2P, 24-Norchola-5,20(22)-dien-3-one 379738-48-4P  
 379738-49-5P, Estra-4,6,16-trien-3-ol 379738-51-9P 379738-52-0P  
 RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
 (steroids as neurochem. stimulators of the VNO to alleviate pain)

IT 53-16-7, reactions 53-43-0 57-63-6 58-22-0 145-13-1 434-22-0  
 474-86-2 517-09-9 1162-53-4 1576-35-8, p-Toluenesulfonylhydrazide  
 2208-12-0 2857-45-6 3604-60-2 6228-47-3, Propyltriphenylphosphonium  
 bromide 13244-39-8 13258-68-9 14030-45-6 14508-15-7,  
 Pregna-4,20-dien-3-one 17879-91-3 21321-88-0 21321-89-1,  
 Pregn-4-en-20-yn-3-one 38388-13-5 38978-06-2 39006-59-2 57597-07-6  
 59452-16-3, 19,21-Dinorchola-1,3,5(10)-trien-3-ol 60149-52-2  
 60149-53-3, 19-Norpregna-4,20-dien-3-one 63015-08-7,  
 Androsta-1,4,16-trien-3-one 71716-18-2 93998-04-0 120574-28-9  
 177349-70-1 177349-71-2 177565-58-1 177794-28-4 178603-56-0  
 RL: RCT (Reactant); RACT (Reactant or reagent)

(steroids as neurochem. stimulators of the VNO to alleviate pain)

IT 1434-85-1P 19865-18-0P 34988-34-6P 55105-93-6P 103614-70-6P,  
 Androsta-5,16-dien-3-one 202718-05-6P  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT  
 (Reactant or reagent)

(steroids as neurochem. stimulators of the VNO to alleviate pain)

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     Premenstrual Syndrome 1980, P31  
 (121) van Lier, J; J Org Chem 1970, V36(8), P2631  
 (122) Veldhuis; J Clin Endocr Metab 1987, V64, P1275 HCPLUS  
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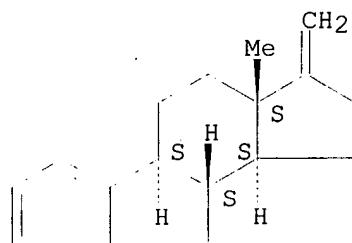
IT 34111-53-OP

RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)  
 (steroids as neurochem. stimulators of the VNO to alleviate pain)

RN 34111-53-0 HCPLUS

CN Estra-1,3,5(10)-trien-3-ol, 17-methylene- (7CI, 8CI, 9CI) (CA INDEX NAME)

Absolute stereochemistry.



HO

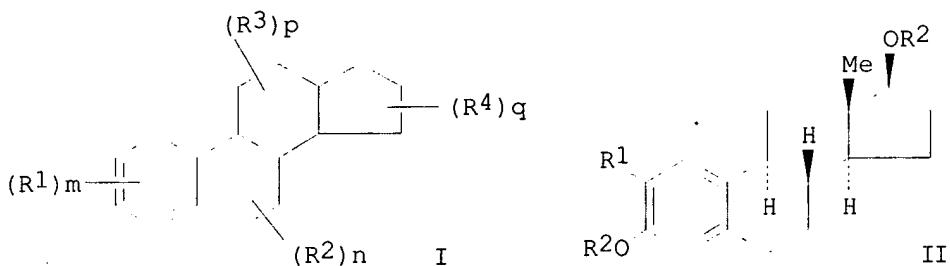
L89 ANSWER 2 OF 22 HCPLUS COPYRIGHT 2003 ACS on STN  
 AN 2001:283974 HCPLUS  
 DN 134:295993  
 ED Entered STN: 20 Apr 2001  
 TI Estradiol conjugates and their therapeutic applications  
 IN Stewart, Alastair George; McAllister, David James; Collis, Maree Patricia;  
     Robertson, Alan Duncan  
 PA University of Melbourne, Australia  
 SO PCT Int. Appl., 57 pp.  
 CODEN: PIXXD2  
 DT Patent  
 LA English  
 IC ICM C07J001-00  
 ICS A61K047-36; A61K047-42; A61K047-48; A61P009-00; A61P035-00  
 CC 32-3 (Steroids)  
 Section cross-reference(s): 1, 2, 33

FAN, CNT 1

PATENT NO.		KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001027132	A1	20010419	WO 2000-AU1244	20001013 <--
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP	1226154	A1	20020731	EP 2000-969105	20001013 <--
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL				
JP	2003511461	T2	20030325	JP 2001-530350	20001013 <--
	ZA 2002002622	A	20030304	ZA 2002-2622	20020404 <--
PRAI	AU 1999-3425	A	19991014 <--		
	WO 2000-AU1244	W	20001013 <--		

OS MARPAT 134:295993

GI



AB The invention discloses the preparation of conjugated prodrug of estradiol compound I ( $R_1-R_4 = H, OH, \text{halo, alkyl, alkenyl, alkynyl, cycloalkyl, amino, aryl, keto, hydrazone, oximino, carbohydrate, peptide, etc.}$ ;  $m,n,p,q = 0-3$ ), a pharmaceutically acceptable salt or in vivo hydrolyzable ester, amide carbonate or carbamate thereof, in the treatment of conditions associated with enhanced angiogenesis or accelerated cell division, such as cancer, and inflammatory conditions such as asthma and rheumatoid arthritis and hyperproliferative skin disorders including psoriasis. Thus, II [ $R_1 = OMe, R_2 = H$  (III)] was prepared via multi-step reaction sequence starting from  $\beta$ -estradiol II ( $R_1-R_2 = H$ ). In human airway fibroblasts thrombin-stimulated increases in cell number were reduced to 12  $\pm$  8% of the control response by III.

ST estradiol conjugate prodrug prep angiogenesis inhibitor

## IT Peptides, preparation

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(conjugates; preparation of peptide conjugated prodrug of estradiol compds. for the treatment of conditions associated with enhanced angiogenesis or accelerated cell division)

## IT Partition

(for the measurement of relative solubilities of estradiol conjugates)

## IT Glycosides

RL: BAC (Biological activity or effector, except adverse); BSU (Biological

- study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
- (glucuronides, estrogenic; preparation of glucuronide prodrug of estradiol compds. for the treatment of conditions associated with enhanced angiogenesis or accelerated cell division)
- IT Estrogens
- RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
- (hydroxy, glucuronides; preparation of glucuronide prodrug of estradiol compds. for the treatment of conditions associated with enhanced angiogenesis or accelerated cell division)
- IT Fluorometry
- (in determination of relative solubilities of estradiol conjugates for the treatment of conditions associated with enhanced angiogenesis or accelerated cell division)
- IT Antitumor agents
- (preparation of conjugated prodrug of estradiol compds. for the treatment of conditions associated with enhanced angiogenesis or accelerated cell division)
- IT Antiasthmatics
- Rheumatoid arthritis
- (preparation of conjugated prodrug of estradiol compds. for the treatment of inflammatory conditions such as asthma and rheumatoid arthritis)
- IT Psoriasis
- (preparation of conjugated prodrug of estradiol compds. for the treatment of psoriasis)
- IT Estrogen receptors
- RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
- (preparation of estradiol conjugates and their binding with rat uterine cytosol estrogen receptor)
- IT DNA formation
- (preparation of estradiol conjugates for regulation of DNA synthesis)
- IT Respiratory tract
- (preparation of estradiol conjugates for regulation of airway mesenchymal cell number)
- IT Angiogenesis inhibitors
- Anti-inflammatory agents
- (preparation of estradiol conjugates for the treatment of conditions associated with enhanced angiogenesis or accelerated cell division)
- IT Estrogens
- RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
- (preparation of estradiol conjugates for the treatment of conditions associated with enhanced angiogenesis or accelerated cell division)
- IT Galactosides
- RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
- (preparation of galactoside prodrug of estradiol compds. for the treatment of conditions associated with enhanced angiogenesis or accelerated cell division)
- IT Drug delivery systems
- (prodrugs; preparation of conjugated prodrug of an estradiol compds. for the treatment of conditions associated with enhanced angiogenesis or

- accelerated cell division)
- IT Proliferation inhibition  
 (proliferation inhibitors; preparation of estradiol conjugates for the treatment of conditions associated with enhanced angiogenesis or accelerated cell division)
- IT Skin, disease  
 (proliferative; preparation of conjugated prodrug of estradiol compds. for the treatment of hyperproliferative skin disorders)
- IT 7291-57-8P 69540-62-1P 334791-42-3P 334791-45-6P  
 334791-46-7P  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)  
 (preparation of estradiol conjugates for the treatment of conditions associated with enhanced angiogenesis or accelerated cell division)
- IT 171064-21-4P 334791-43-4P 334791-47-8P 334791-49-0P  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
 (preparation of estradiol conjugates for the treatment of conditions associated with enhanced angiogenesis or accelerated cell division)
- IT 9001-45-0,  $\beta$ -Glucuronidase  
 RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)  
 (preparation of estradiol conjugates for the treatment of conditions associated with enhanced angiogenesis or accelerated cell division)
- IT 52717-98-3P  
 RL: BYP (Byproduct); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
 (preparation of estradiol conjugates for the treatment of conditions associated with enhanced angiogenesis or accelerated cell division)
- IT 513-78-0, Cadmium carbonate  
 RL: CAT (Catalyst use); USES (Uses)  
 (preparation of estradiol conjugates for the treatment of conditions associated with enhanced angiogenesis or accelerated cell division)
- IT 50-28-2,  $\beta$ -Estradiol, reactions 100-39-0, Benzyl bromide  
 108-24-7, Acetic anhydride 3068-32-4 7803-57-8, Hydrazine hydrate 21085-72-3  
 RL: RCT (Reactant); RACT (Reactant or reagent)  
 (preparation of estradiol conjugates for the treatment of conditions associated with enhanced angiogenesis or accelerated cell division)
- IT 362-07-2P 69455-04-5P 69540-63-2P 83274-89-9P 159143-75-6P  
 159143-76-7P 192062-05-8P 334791-44-5P  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
 (preparation of estradiol conjugates for the treatment of conditions associated with enhanced angiogenesis or accelerated cell division)
- RE.CNT 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD  
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 (12) Watanabe, K; Chem Pharm Bull 1982, V30(9), P3231 HCAPLUS

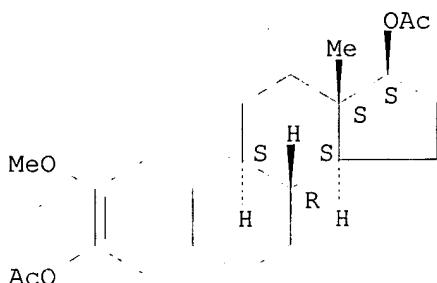
IT 7291-57-8P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)  
 (preparation of estradiol conjugates for the treatment of conditions associated with enhanced angiogenesis or accelerated cell division)

RN 7291-57-8 HCAPLUS

CN Estra-1,3,5(10)-triene-3,17-diol, 2-methoxy-, diacetate, (17 $\beta$ )- (9CI)  
 (CA INDEX NAME)

Absolute stereochemistry.



L89 ANSWER 3 OF 22 HCAPLUS COPYRIGHT 2003 ACS on STN

AN 2000:635218 HCAPLUS

DN 133:208036

ED Entered STN: 13 Sep 2000

TI Preparation of steroids as neurochemical stimulators of the VNO to alleviate symptoms of PMS and anxiety

IN Jennings-white, Clive L.; Berliner, David L.; Adams, Nathan W.; Monti-bloch, Luis

PA Pherin Pharmaceuticals, Inc., USA

SO U.S., 299 pp., Cont.-in-part of U.S. Ser. No. 725,862.

CODEN: USXXAM

DT Patent

LA English

IC ICM A61K031-56

NCL 514177000

CC 32-3 (Steroids)

Section cross-reference(s): 2, 63

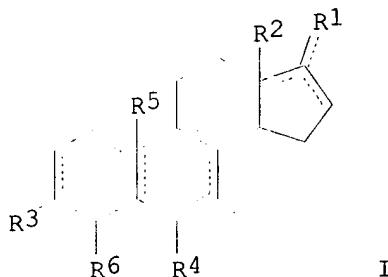
FAN.CNT 12

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 6117860	A	20000912	US 1997-899094	19970723 <--
	US 5563131	A	19961008	US 1994-286073	19940804 <--
	US 6066627	A	20000523	US 1996-625268	19960329 <--
	US 6057439	A	20000502	US 1996-686092	19960723 <--
	WO 9814194	A1	19980409	WO 1997-US18086	19971006 <--
	W:	AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			

RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR,  
 GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA,  
 GN, ML, MR, NE, SN, TD, TG

AU 9748103	A1 19980424	AU 1997-48103	19971006 <--
PRAI US 1994-286073	A2 19940804 <--		
US 1996-625268	A2 19960329 <--		
US 1996-686092	A2 19960723 <--		
US 1996-725862	A2 19961004 <--		
US 1997-899094	A 19970723 <--		
WO 1997-US18086	W 19971006 <--		

OS MARPAT 133:208036  
 GI



- AB The invention relates to a method of alleviating the symptoms of PMS and anxiety. The method comprises nasally administering a steroid which is a human vomeropherin, e.g. a compound of formula I [R<sub>1</sub> = H, Me, CH<sub>2</sub>, halo; R<sub>2</sub> = absent, H, Me; R<sub>3</sub> = oxo, OH, alkoxy, acyloxy, benzoyl, etc.; R<sub>4</sub> = H, OH, alkoxy, acyloxy, oxo, halo; R<sub>5</sub> = absent, H, OH, alkoxy, acyloxy; R<sub>6</sub> = H, halo], such that the vomeropherin binds to a specific neuroepithelial receptor. Thus, 10 $\beta$ -hydroxy-16 $\alpha$ ,17 $\alpha$ -epoxyestr-4-en-3-one is prepared from estra 5(10),16-dien-3-one, and is used in pharmaceutical compns. The compds. of the invention are tested for their effect on EEG and autonomic activity in women and men. The steroid or steroids is/are preferably administered in the form of a pharmaceutical composition containing one or more pharmaceutically acceptable carriers.
- ST steroid prepn neurochem stimulator VNO; estrene prepn neurochem stimulator VNO; PMS treatment steroid prepn; premenstrual dysphoric disorder treatment steroid prepn; anxiety treatment steroid prepn; neuroepithelial receptor steroid prepn
- IT Reflex  
 (autonomic; preparation of steroids as neurochem. stimulators of VNO to alleviate symptoms of PMS and anxiety)
- IT Brain  
 (hypothalamus; preparation of steroids as neurochem. stimulators of VNO to alleviate symptoms of PMS and anxiety)
- IT Fertility  
 (inhibitors; preparation of steroids as neurochem. stimulators of VNO to alleviate symptoms of PMS and anxiety)
- IT Drug delivery systems  
 (nasal; preparation of steroids as neurochem. stimulators of VNO to alleviate symptoms of PMS and anxiety)
- IT Receptors  
 RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)  
 (neuroepithelial; preparation of steroids as neurochem. stimulators of VNO to alleviate symptoms of PMS and anxiety)

IT Ovarian cycle  
 (premenstrual syndrome, treatment; preparation of steroids as neurochem. stimulators of VNO to alleviate symptoms of PMS and anxiety)

IT Antitumor agents  
 Anxiolytics  
 (preparation of steroids as neurochem. stimulators of VNO to alleviate symptoms of PMS and anxiety)

IT Steroids, preparation  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
 (preparation of steroids as neurochem. stimulators of VNO to alleviate symptoms of PMS and anxiety)

IT Nose  
 (vomeronasal organ; preparation of steroids as neurochem. stimulators of VNO to alleviate symptoms of PMS and anxiety)

IT 1150-90-9P, Estra-1,3,5(10),16-tetraen-3-ol 4736-62-3P 35581-65-8P,  
 Pregna-4,16-dien-3-one 65754-63-4P, Pregna-1,4,20-trien-3-one  
 71496-98-5P, Estra-4,16-dien-3-one 97560-70-8P, 19-Norpregna-  
 1,3,5(10),20-tetraen-3-ol 99898-92-7P, 19-Norpregna-1,3,5(10)-trien-20-  
 yn-3-ol 99898-93-8P 105663-60-3P 161061-73-0P 161061-81-0P  
 161061-82-1P 177349-45-0P 177349-52-9P 177349-64-3P 177349-66-5P  
 177565-58-1P 186183-19-7P, 19-Norpregna-5(10),20-dien-3-one  
 186183-25-5P 250683-25-1P  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)  
 (preparation of steroids as neurochem. stimulators of VNO to alleviate symptoms of PMS and anxiety)

IT 2118-31-2 14030-45-6 14508-15-7, Pregna-4,20-dien-3-one 16377-13-2  
 21321-88-0 28336-31-4 60149-52-2 60149-53-3, 19-Norpregna-4,20-dien-  
 3-one 71016-68-7 93998-04-0 177349-71-2 202718-08-9 202718-10-3  
 205994-34-9  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); THU (Therapeutic use); BIOL (Biological study); RACT (Reactant or reagent); USES (Uses)  
 (preparation of steroids as neurochem. stimulators of VNO to alleviate symptoms of PMS and anxiety)

IT 472-56-0P 1232-18-4P, Pregn-4-en-3-one 2862-58-0P,  
 Pregn-5-en-3 $\beta$ -ol 21321-95-9P 23062-06-8P 23640-47-3P  
 26400-72-6P 30505-67-0P 58594-49-3P 71716-18-2P 86306-63-0P  
 86306-96-9P 120476-05-3P 161061-71-8P 161061-72-9P 161061-83-2P  
 161061-84-3P 161061-99-0P, Estra-4,9,16-trien-3-one 161062-01-7P  
 161062-02-8P 161062-04-0P, Estra-1,3,5(10),7-tetraen-3-ol 161062-05-1P  
 161062-09-5P 177349-46-1P 177349-48-3P, 24-Norchola-4,20(22)-dien-3,6-  
 dione 177349-49-4P, 24-Norchola-4,20(22)-dien-3-one 177349-53-0P  
 177349-54-1P 177349-55-2P 177349-56-3P, Pregna-4,16-diene-3,6-dione  
 177349-57-4P, Pregna-4,17(20),20-triene-3,6-dione 177349-59-6P  
 177349-60-9P, 24-Norchola-4,22-diene-3,6-dione 177349-61-0P  
 177349-62-1P 177349-63-2P 177349-65-4P 177349-67-6P 177349-68-7P  
 177349-69-8P 177349-72-3P, Pregna-1,4,20-trien-3-ol 177349-73-4P,  
 Pregna-4,20-diene-3,6-dione 177695-29-3P 177794-21-7P 177794-22-8P  
 177794-23-9P 177794-24-0P 177794-26-2P 177794-27-3P 177794-31-9P  
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 177856-19-8P 177856-20-1P 177856-21-2P 177856-22-3P 177856-23-4P  
 178033-52-8P, Estra-1,3,5(10),16-tetraene-3,6-diol 178033-53-9P,  
 Estra-4,16-dien-3-ol 186183-17-5P 186183-18-6P 186183-21-1P  
 186183-22-2P, 19-Norpregna-4,9,20-trien-3-one 186183-26-6P  
 186183-27-7P 186183-28-8P 186183-29-9P 190596-13-5P,  
 Estra-5(10),16-dien-3-ol 200511-34-8P 200574-68-1P,  
 19,21-Dinorchol-4-en-3-one 202718-04-5P 211123-94-3P 265313-78-8P  
 265313-81-3P 265313-82-4P 265313-83-5P 265313-84-6P 265313-85-7P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
 (preparation of steroids as neurochem. stimulators of VNO to alleviate symptoms of PMS and anxiety)

IT 53-16-7, Estrone, reactions 53-43-0 57-63-6, Ethynylestradiol  
 58-22-0, Testosterone 145-13-1 434-22-0, 19-Nortestosterone  
 474-86-2, Equilin 517-09-9, Equilenin 1162-53-4 1624-62-0  
 2208-12-0, 6-Dehydroestrone 2857-45-6 3604-60-2 13244-39-8  
 13258-68-9, Ethynylestradiol diacetate 16397-00-5 17879-91-3  
 21321-89-1, Pregn-4-en-20-yn-3-one 33767-87-2 38388-13-5 38978-06-2  
 39006-59-2 57597-07-6 63015-08-7, Androsta-1,4,16-trien-3-one  
 120574-28-9 177349-70-1 178603-56-0 215732-74-4

RL: RCT (Reactant); RACT (Reactant or reagent)  
 (preparation of steroids as neurochem. stimulators of VNO to alleviate symptoms of PMS and anxiety)

IT 846-45-7P 1224-94-8P 4075-07-4P, Androsta-4,16-dien-3-one 7628-02-6P  
 19865-18-0P 34111-53-0P 34988-34-6P 35456-72-5P  
 55105-93-6P, Estrone p-toluenesulfonylhydrazone 59452-16-3P,  
 19,21-Dinorchola-1,3,5(10)-trien-3-ol 71683-67-5P 77257-06-8P  
 86306-95-8P 103614-70-6P, Androsta-5,16-dien-3-one 105644-55-1P  
 161061-70-7P 161061-86-5P 161061-93-4P 161061-95-6P 161061-97-8P  
 161061-98-9P, Estra-5(10),16-dien-3-one 161062-00-6P 177349-50-7P  
 177349-51-8P 177349-58-5P, 24-Norchola-4,22-dien-3-one 177349-74-5P  
 177794-25-1P 177794-29-5P 177794-30-8P 177856-06-3P 177856-07-4P,  
 Estra-1,3,5(10),6,16-pentaen-3-ol 177856-09-6P 177856-10-9P,  
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 200511-39-3P 200511-50-8P, 19,21-Dinorchola-5(10),16-dien-3-one  
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RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
 (preparation of steroids as neurochem. stimulators of VNO to alleviate symptoms of PMS and anxiety)

RE.CNT 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD

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- (3) Anon; DE 854517 1952 HCPLUS
- (4) Anon; FR 1363191 1963 HCPLUS
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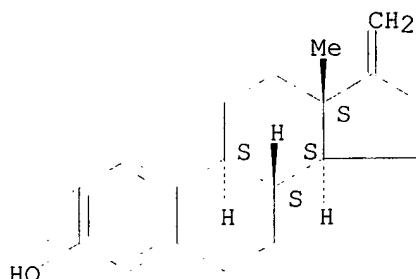
IT 34111-53-0P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
 (preparation of steroids as neurochem. stimulators of VNO to alleviate symptoms of PMS and anxiety)

RN 34111-53-0 HCPLUS

CN Estra-1,3,5(10)-trien-3-ol, 17-methylene- (7CI, 8CI, 9CI) (CA INDEX NAME)

Absolute stereochemistry.



L89 ANSWER 4 OF 22 HCPLUS COPYRIGHT 2003 ACS on STN

AN 2000:344112 HCPLUS

DN 132:347795

ED Entered STN: 24 May 2000

TI Preparation of steroids as neurochemical initiators of change in human blood levels of LH

IN Jennings-White, Clive L.; Berliner, David L.; Adams, Nathan W.

PA Pherin Corporation, USA

SO U.S., 255 pp., Cont.-in-part of U.S. 5,563,131.

CODEN: USXXAM

DT Patent

LA English

IC ICM A61K031-56

NCL 514177000

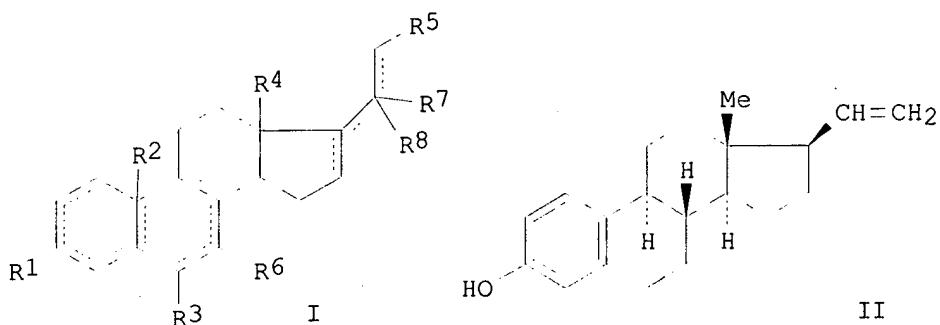
CC 32-5 (Steroids)

Section cross-reference(s): 2

FAN.CNT 12

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 6066627	A	20000523	US 1996-625268	19960329 <--
	US 5563131	A	19961008	US 1994-286073	19940804 <--
	HU 77600	A2	19980629	HU 1997-327	19950804 <--
	US 6057439	A	20000502	US 1996-686092	19960723 <--
	CA 2250309	AA	19971009	CA 1997-2250309	19970328 <--
	WO 9736596	A1	19971009	WO 1997-US6061	19970328 <--
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LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT,  
 RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, UZ, VN, AM,  
 AZ, BY, KG, KZ, MD, RU, TJ, TM  
 RW: GH, KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB,  
 GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN,  
 ML, MR, NE, SN, TD, TG  
 AU 9726650 A1 19971022 AU 1997-26650 19970328 <--  
 AU 735804 B2 20010712  
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 US 1996-625268 A2 19960329 <--  
 US 1996-686092 A2 19960723 <--  
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 WO 1997-US6061 W 19970328 <--  
 OS MARPAT 132:347795  
 GI



AB The invention relates to a method of altering the blood levels of LH or FSH in an individual. The method comprises nasally administering a steroid which is a human vomeropherin, such that the vomeropherin binds to a specific neuroepithelial receptor. Steroids, e.g. of formula I [R1 = oxo, OH, OAc, propionyloxy, alkoxy, acyloxy, benzyloxy; R2 = H, OH, alkoxy, absent; R3 = oxo, OH, alkoxy, halo; R4 = Me, Et; R5 = H, Me, halo; R6 = H, Me; R7, R8 = H, halo, absent], are prepared as vomerophersins. Thus, II was prepared from ethynodiol diacetate. The prepared 19-norpregnane vomerophersins were tested for autonomic activity in women.

ST neurochem initiator LH blood level steroid prep; FSH blood level neurochem initiator steroid prep; anxiolytic steroid vomeropherin prep; hypothalamic function steroid vomeropherin prep

IT Brain  
 (hypothalamus; preparation of steroids as neurochem. initiators of change in human blood levels of LH)

IT Fertility  
 (inhibitors; preparation of steroids as neurochem. initiators of change in human blood levels of LH)

IT Drug delivery systems  
 (nasal; preparation of steroids as neurochem. initiators of change in human blood levels of LH)

IT Anxiolytics  
 (preparation of steroids as neurochem. initiators of change in human blood levels of LH)

## IT Steroids, preparation

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
 (preparation of steroids as neurochem. initiators of change in human blood levels of LH)

## IT Nose

(vomeronasal organ; preparation of steroids as neurochem. initiators of change in human blood levels of LH)

IT 846-45-7P 1150-90-9P, Estra-1,3,5(10),16-tetraen-3-ol 1224-94-8P

4075-07-4P, Androsta-4,16-dien-3-one 34111-53-0P 35456-72-5P  
 65754-63-4P, Pregna-1,4,20-trien-3-one 71496-98-5P, Estra-4,16-dien-3-one 77257-06-8P 86306-95-8P 97560-70-8P, 19-Norpregna-1,3,5(10),20-tetraen-3-ol 99898-93-8P 161061-70-7P 161061-73-0P 161061-86-5P  
 161061-93-4P 161061-95-6P 161061-97-8P 161061-98-9P,  
 Estra-5(10),16-dien-3-one 161062-00-6P 177349-45-0P 177349-50-7P  
 177349-51-8P 177349-52-9P 177349-58-5P, 24-Norchola-4,22-dien-3-one  
 177349-64-3P 177349-66-5P 177349-74-5P 177565-58-1P 177794-25-1P  
 177794-29-5P 177794-30-8P 177856-06-3P 177856-07-4P,  
 Estra-1,3,5(10),6,16-pentaen-3-ol 177856-09-6P 177856-10-9P,  
 Estra-1,3,5(10),7,16-pentaen-3-ol 177856-12-1P 177856-13-2P,  
 Estra-1,3,5,7,9,16-hexaen-3-ol 177856-15-4P 177856-17-6P  
 177856-18-7P 186183-19-7P, 19-Norpregna-5(10),20-dien-3-one  
 186183-25-5P 250683-25-1P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)  
 (preparation of steroids as neurochem. initiators of change in human blood levels of LH)

IT 2118-31-2 14030-45-6 14508-15-7, Pregna-4,20-dien-3-one 21321-88-0

28336-31-4 60149-52-2 60149-53-3, 19-Norpregna-4,20-dien-3-one  
 71716-18-2

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); THU (Therapeutic use); BIOL (Biological study); RACT (Reactant or reagent); USES (Uses)  
 (préparation of steroids as neurochem. initiators of change in human blood levels of LH)

IT 53-63-4P, Estra-1,3,5(10)-trien-3-ol 1232-18-4P, Pregn-4-en-3-one  
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 58594-49-3P 59077-04-2P, 19-Norpregna-1,3,5(10)-trien-3-ol  
 63014-91-5P, Androsta-4,6,16-trien-3-one 86306-63-0P 86306-96-9P  
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 177349-54-1P 177349-55-2P 177349-56-3P, Pregna-4,16-diene-3,6-dione  
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250683-26-2P, 24-Norchola-5,20(22)-dien-3-one 269080-35-5P  
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 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
 (preparation of steroids as neurochem. initiators of change in human blood levels of LH)

IT 9002-67-9, LH 9002-68-0, FSH  
 RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)  
 (preparation of steroids as neurochem. initiators of change in human blood levels of LH)

IT 53-16-7, Estrone, reactions 53-43-0 57-63-6, Ethynylestradiol  
 58-22-0, Testosterone 145-13-1 434-22-0, 19-Nortestosterone  
 474-86-2, Equilin 517-09-9, Equilenin 1162-53-4 2208-12-0,  
 6-Dehydroestrone 2857-45-6 3604-60-2, Ethynodioldecanoate  
 13244-39-8 13258-68-9, Ethynylestradiol diacetate 17879-91-3  
 21321-89-1, Pregn-4-en-20-yn-3-one 38388-13-5 38978-06-2 39006-59-2  
 57597-07-6 63015-08-7, Androsta-1,4,16-trien-3-one 93998-04-0  
 177349-70-1 177349-71-2 177794-28-4 178603-56-0  
 RL: RCT (Reactant); RACT (Reactant or reagent)  
 (preparation of steroids as neurochem. initiators of change in human blood levels of LH)

IT 19865-18-0P 33767-87-2P 34988-34-6P 55105-93-6P, Estrone  
 p-toluenesulfonylhydrazone 103614-70-6P, Androsta-5,16-dien-3-one  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
 (preparation of steroids as neurochem. initiators of change in human blood levels of LH)

RE.CNT 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS RECORD

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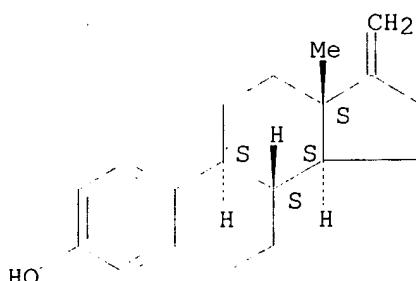
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RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)  
 (preparation of steroids as neurochem. initiators of change in human blood levels of LH)

RN 34111-53-0 HCAPLUS

CN Estra-1,3,5(10)-trien-3-ol, 17-methylene- (7CI, 8CI, 9CI) (CA INDEX NAME)

Absolute stereochemistry.



L89 ANSWER 5 OF 22 HCAPLUS COPYRIGHT 2003 ACS on STN

AN 2000:284021 HCAPLUS

DN 132:308544

ED Entered STN: 03 May 2000

TI Preparation of steroids as neurochemical stimulators of the VNO to alleviate symptoms of PMS and anxiety

IN Jennings-white, Clive L.; Berliner, David L.; Adams, Nathan W.; Monti-bloch, Luis

PA Pherin Corporation, USA

SO U.S., 284 pp., Cont.-in-part of U.S. Ser. No. 625,268.

CODEN: USXXAM

DT Patent

LA English

IC C07J005-00

NCL 540024000

CC 32-3 (Steroids)

Section cross-reference(s): 2, 63

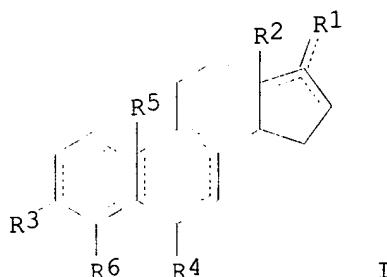
FAN.CNT 12

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	US 6066627	A	20000523	US 1996-625268	19960329 <--
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 RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN,  
 YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM  
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 GN, ML, MR, NE, SN, TD, TG

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US 6117860	A	20000912	US 1997-899094	19970723 <--
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US 1996-686092	A	19960723	<--	
US 1996-725862	A	19961004	<--	
WO 1997-US13035	W	19970723	<--	

GI



- AB The invention relates to a method of alleviating the symptoms of PMS and anxiety. The method comprises nasally administering a steroid which is a human vomeropherin, e.g. a compound of formula I [R1 = H, Me, CH<sub>2</sub>, halo; R2 = absent, H, Me; R3 = oxo, OH, alkoxy, acyloxy, benzoyl, etc.; R4 = H, OH, alkoxy, acyloxy, oxo, halo; R5 = absent, H, OH, alkoxy, acyloxy; R6 = H, halo], such that the vomeropherin binds to a specific neuroepithelial receptor. Thus, 10β-hydroxy-16α,17α-epoxyestr-4-en-3-one is prepared from estra 5(10),16-dien-3-one, and is used in pharmaceutical compns. The compds. of the invention are tested for their effect on EEG and autonomic activity in women and men. The steroid or steroids is/are preferably administered in the form of a pharmaceutical composition containing one or more pharmaceutically acceptable carriers.
- ST steroid prepn neurochem stimulator VNO; estrene prepn neurochem stimulator VNO; PMS treatment steroid prepn; premenstrual dysphoric disorder treatment steroid prepn; anxiety treatment steroid prepn; neuroepithelial receptor steroid prepn
- IT Reflex  
 (autonomic; preparation of steroids as neurochem. stimulators of VNO to alleviate symptoms of PMS and anxiety)
- IT Brain  
 (hypothalamus; preparation of steroids as neurochem. stimulators of VNO to alleviate symptoms of PMS and anxiety)

IT Fertility  
 (inhibitors; preparation of steroids as neurochem. stimulators of VNO to alleviate symptoms of PMS and anxiety)

IT Drug delivery systems  
 (nasal; preparation of steroids as neurochem. stimulators of VNO to alleviate symptoms of PMS and anxiety)

IT Receptors  
 RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)  
 (neuroepithelial; preparation of steroids as neurochem. stimulators of VNO to alleviate symptoms of PMS and anxiety)

IT Ovarian cycle  
 (premenstrual syndrome, treatment; preparation of steroids as neurochem. stimulators of VNO to alleviate symptoms of PMS and anxiety)

IT Antitumor agents  
 Anxiolytics  
 (preparation of steroids as neurochem. stimulators of VNO to alleviate symptoms of PMS and anxiety)

IT Steroids, preparation  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
 (preparation of steroids as neurochem. stimulators of VNO to alleviate symptoms of PMS and anxiety)

IT Nose  
 (vomeronasal organ; preparation of steroids as neurochem. stimulators of VNO to alleviate symptoms of PMS and anxiety)

IT 1150-90-9P, Estra-1,3,5(10),16-tetraen-3-ol 65754-63-4P,  
 Pregna-1,4,20-trien-3-one 71496-98-5P, Estra-4,16-dien-3-one  
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 186183-25-5P 250683-25-1P  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)  
 (preparation of steroids as neurochem. stimulators of VNO to alleviate symptoms of PMS and anxiety)

IT 2118-31-2 14030-45-6 14508-15-7, Pregna-4,20-dien-3-one 21321-88-0  
 28336-31-4 60149-52-2 60149-53-3, 19-Norpregna-4,20-dien-3-one  
 93998-04-0 177349-71-2  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); THU (Therapeutic use); BIOL (Biological study); RACT (Reactant or reagent); USES (Uses)  
 (preparation of steroids as neurochem. stimulators of VNO to alleviate symptoms of PMS and anxiety)

IT 472-56-0P 1232-18-4P, Pregn-4-en-3-one 2862-58-0P,  
 Pregn-5-en-3 $\beta$ -ol 4736-62-3P 21321-95-9P 23062-06-8P  
 23640-47-3P 26400-72-6P 30505-67-0P 35581-65-8P,  
 Pregna-4,16-dien-3-one 58594-49-3P 71716-18-2P 86306-63-0P  
 86306-96-9P 120476-05-3P 161061-71-8P 161061-72-9P 161061-83-2P  
 161061-84-3P 161061-99-0P, Estra-4,9,16-trien-3-one 161062-01-7P  
 161062-02-8P 161062-04-0P, Estra-1,3,5(10),7-tetraen-3-ol 161062-05-1P  
 161062-09-5P 177349-46-1P 177349-48-3P, 24-Norchola-4,20(22)-diene-3,6-dione  
 177349-49-4P, 24-Norchola-4,20(22)-dien-3-one 177349-53-0P  
 177349-54-1P 177349-55-2P 177349-56-3P, Pregna-4,16-diene-3,6-dione  
 177349-57-4P, Pregna-4,17(20),20-triene-3,6-dione 177349-59-6P  
 177349-60-9P, 24-Norchola-4,22-diene-3,6-dione 177349-61-0P  
 177349-62-1P 177349-63-2P 177349-65-4P 177349-67-6P 177349-68-7P  
 177349-69-8P 177349-72-3P, Pregna-1,4,20-trien-3-ol 177349-73-4P,  
 Pregna-4,20-diene-3,6-dione 177695-29-3P 177794-21-7P 177794-22-8P

177794-23-9P 177794-24-0P 177794-26-2P 177794-27-3P 177794-31-9P  
 177794-32-0P 177856-08-5P 177856-11-0P 177856-14-3P 177856-16-5P  
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 Estra-5(10),16-dien-3-ol 200511-34-8P 200574-68-1P,  
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 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
 (preparation of steroids as neurochem. stimulators of VNO to alleviate symptoms of PMS and anxiety)

IT 53-16-7, Estrone, reactions 53-43-0 57-63-6, Ethynylestradiol  
 58-22-0, Testosterone 145-13-1 434-22-0, 19-Nortestosterone  
 474-86-2, Equilin 517-09-9, Equilenin 1162-53-4 2208-12-0,  
 6-Dehydroestrone 2857-45-6 3604-60-2 13244-39-8 13258-68-9,  
 Ethynylestradiol diacetate 17879-91-3 21321-89-1, Pregn-4-en-20-yn-3-one 33767-87-2 38388-13-5 38978-06-2 39006-59-2 57597-07-6  
 63015-08-7, Androsta-1,4,16-trien-3-one 120574-28-9 177349-70-1  
 178603-56-0 215732-74-4  
 RL: RCT (Reactant); RACT (Reactant or reagent)  
 (preparation of steroids as neurochem. stimulators of VNO to alleviate symptoms of PMS and anxiety)

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 19865-18-0P 34111-53-0P 34988-34-6P 35456-72-5P  
 55105-93-6P, Estrone p-toluenesulfonylhydrazone 59452-16-3P,  
 19,21-Dinorchola-1,3,5(10)-trien-3-ol 77257-06-8P 86306-95-8P  
 103614-70-6P, Androsta-5,16-dien-3-one 161061-70-7P 161061-86-5P  
 161061-93-4P 161061-95-6P 161061-97-8P 161061-98-9P,  
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 177794-29-5P 177794-30-8P 177856-06-3P 177856-07-4P,  
 Estra-1,3,5(10),6,16-pentaen-3-ol 177856-09-6P 177856-10-9P,  
 Estra-1,3,5(10),7,16-pentaen-3-ol 177856-12-1P 177856-13-2P,  
 Estra-1,3,5,7,9,16-hexaen-3-ol 177856-15-4P 177856-17-6P  
 177856-18-7P 178688-50-1P 200511-32-6P 200511-37-1P 200511-39-3P  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
 (preparation of steroids as neurochem. stimulators of VNO to alleviate symptoms of PMS and anxiety)

RE.CNT 119 THERE ARE 119 CITED REFERENCES AVAILABLE FOR THIS RECORD

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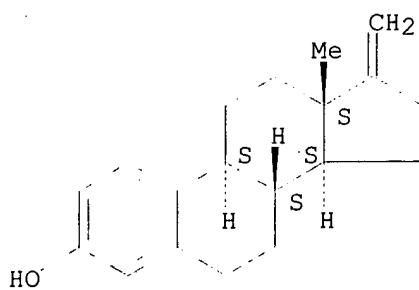
IT 34111-53-0P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
 (preparation of steroids as neurochem. stimulators of VNO to alleviate symptoms of PMS and anxiety)

RN 34111-53-0 HCPLUS

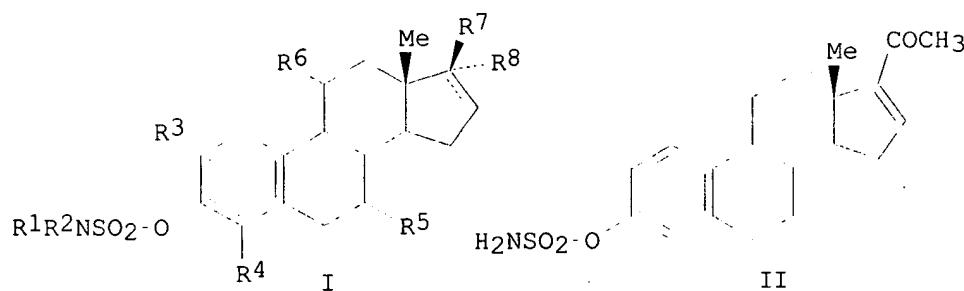
CN Estra-1,3,5(10)-trien-3-ol, 17-methylene- (7CI, 8CI, 9CI) (CA INDEX NAME)

Absolute stereochemistry.



L89 ANSWER 6 OF 22 HCAPLUS COPYRIGHT 2003 ACS on STN  
 AN 1999:460438 HCAPLUS  
 DN 131:88083  
 ED Entered STN: 28 Jul 1999  
 TI Preparation of estrone sulfamate inhibitors of estrone sulfatase  
 IN Tanabe, Masato; Peters, Richard H.; Chao, Wan-Ru; Shigeno, Kazuhiko  
 PA SRI International, USA  
 SO PCT Int. Appl., 102 pp.  
 CODEN: PIXXD2  
 DT Patent  
 LA English  
 IC ICM C07J041-00  
 ICS A61K031-565; A61K031-57; A61K031-575  
 CC 32-3 (Steroids)  
 Section cross-reference(s): 2, 63

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9933858	A2	19990708	WO 1998-US27333	19981221 <--
	W: AU, CA, JP, KR RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	US 6046186	A	20000404	US 1997-997416	19971224 <--
	CA 2318349	AA	19990708	CA 1998-2318349	19981221 <--
	AU 9919416	A1	19990719	AU 1999-19416	19981221 <--
	AU 751732	B2	20020829		
	EP 1042354	A2	20001011	EP 1998-964243	19981221 <--
	R: DE, FR, GB, IT, NL				
	JP 2001527089	T2	20011225	JP 2000-526534	19981221 <--
PRAI	US 1997-997416	A	19971224 <--		
	WO 1998-US27333	W	19981221 <--		
OS	MARPAT 131:88083				
GI					



AB Novel compds.of formula I [R1, R2 = H, alkyl, etc.; R3 = H, CN, NO2, COOH,

alkoxycarbonyl, etc.; R4 = H, NO<sub>2</sub>, (substituted) amino; R5, R6 = H, alkyl; R7, R8 = H, alkyl, alkenyl, alkynyl, alkoxy, acyl, acyloxy, etc.; R7,R8 = oxo, alkylidene, etc.) are prepared as inhibitors of estrone sulfatase. Thus, II is prepared from ethynylestradiol in 4 steps. and showed estrone sulfatase inhibitory activity of IC<sub>50</sub> = 21 pM. Pharmaceutical compns. and methods for using I to treat estrogen-dependent disorders are provided.

ST      estrone sulfamate prepn estrone sulfatase inhibitor

IT      Estrogens  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
 (antiestrogens; preparation of estrone sulfamates as inhibitors of estrone sulfatase)

IT      Antitumor agents  
 (preparation of estrone sulfamates as inhibitors of estrone sulfatase)

IT      59298-96-3, Estrone sulfatase  
 RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)  
 (inhibitors; preparation of estrone sulfamates as inhibitors of estrone sulfatase)

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 229485-79-4P    229485-80-7P    229485-81-8P    229485-82-9P    229485-83-0P  
 229485-84-1P    229485-85-2P    229485-86-3P    229485-87-4P    229485-88-5P  
 229485-89-6P    229485-90-9P    229485-91-0P    229485-92-1P    229485-93-2P  
 229485-94-3P    229485-95-4P    229485-96-5P    229485-97-6P    229485-98-7P  
 229485-99-8P    229486-00-4P    229486-01-5P    229486-02-6P    229486-03-7P  
 229486-04-8P    229486-05-9P  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
 (preparation of estrone sulfamates as inhibitors of estrone sulfatase)

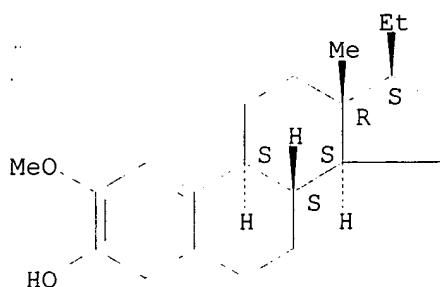
IT      50-28-2, Estradiol, reactions    53-16-7, Estrone, reactions    57-63-6,  
 Ethynylestradiol    108-01-0, N,N-Dimethylethanolamine    109-77-3,  
 Malononitrile    362-08-3    867-13-0, Triethylphosphonoacetate    1779-51-7,  
 Butyltriphenylphosphonium bromide    4584-46-7    5407-04-5    6228-47-3,  
 Propyltriphenylphosphonium bromide    7678-95-7    67530-18-1    229486-27-5  
 RL: RCT (Reactant); RACT (Reactant or reagent)  
 (preparation of estrone sulfamates as inhibitors of estrone sulfatase)

IT      858-98-0P    1667-98-7P    4736-62-3P    5774-17-4P    5779-47-5P    5976-73-8P  
 5976-74-9P    6599-97-9P    13879-55-5P    13879-57-7P    14030-45-6P  
 14846-63-0P    14982-15-1P    15001-40-8P    22787-09-3P    23880-59-3P  
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 59452-15-2P    59452-16-3P, 19,21-Dinorchola-1,3,5(10)-trien-3-ol  
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 115208-23-6P    115387-92-3P    116627-15-7P    116627-20-4P    120574-27-8P  
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 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
 (preparation of estrone sulfamates as inhibitors of estrone sulfatase)

IT      229486-18-4P  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
 (preparation of estrone sulfamates as inhibitors of estrone sulfatase)

RN      229486-18-4    HCAPLUS  
 CN      19-Norpregna-1,3,5(10)-trien-3-ol, 2-methoxy- (9CI)    (CA INDEX NAME)

Absolute stereochemistry.



L89 ANSWER 7 OF 22 HCAPLUS COPYRIGHT 2003 ACS on STN

AN 1998:397783 HCAPLUS

DN 129:54482

ED Entered STN: 29 Jun 1998

TI Preparation of steroid inhibitors of estrone sulfatase and associated pharmaceutical compositions and methods of use

IN Tanabe, Masato; Peters, Richard H.; Chao, Wan-ru; Shigeno, Kazuhiko

PA SRI International, USA

SO U.S., 23 pp.

CODEN: USXXAM

DT Patent

LA English

IC ICM A61K031-58

ICS C07J071-00

NCL 514176000

CC 32-3 (Steroids)

Section cross-reference(s): 1, 2

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 5763432	A	19980609	US 1997-794229	19970129 <--
	US 5861388	A	19990119	US 1997-1601	19971231 <--
	WO 9832763	A1	19980730	WO 1998-US1846	19980129 <--

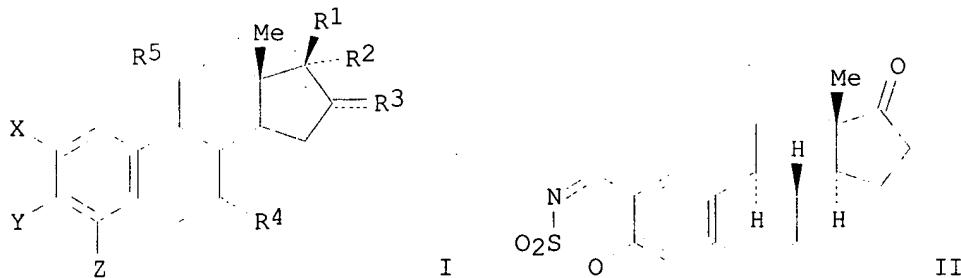
W: CA, JP, KR

RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE

PRAI US 1997-794229 19970129 <--

OS MARPAT 129:54482

GI



AB Estratriene derivs. of formula I [X and Y, or Y and Z, form an oxathiazine dioxide ring or a dihydro-oxathiazine dioxide ring; R1, R2 = H, alkyl, alkynyl, (substituted) OH; R1R2 = O, S, (substituted) CH2; R3 = H, halo, alkyl, CH2; R4 = H, alkyl; R5 = H, OH, alkyl, alkenyl, alkoxy, aryl, CH2] are prepared as inhibitors of estrone sulfatase. Pharmaceutical compns. and methods for using I to treat estrogen-dependent disorders are provided as

well. Thus, estradiol is transformed into II in 3 steps. In an estrone sulfatase inhibition assay, II showed 5% inhibition at 9.3 nM.

ST estratriene deriv prepn estrone sulfatase inhibitor  
IT 208758-20-7P 208758-22-9P  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)  
(preparation of steroid inhibitors of estrone sulfatase)

IT 208758-16-1P 208758-17-2P 208758-21-8P 208758-23-0P 208758-25-2P  
208758-33-2P 208758-34-3P 208758-35-4P 208758-36-5P 208758-37-6P  
208758-38-7P 208758-39-8P 208758-41-2P 208758-43-4P 208758-48-9P  
208758-52-5P 208758-54-7P  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
(preparation of steroid inhibitors of estrone sulfatase)

IT 59298-96-3, Estrone sulfatase  
RL: BPR (Biological process); BSU (Biological study, unclassified); MSC (Miscellaneous); BIOL (Biological study); PROC (Process)  
(preparation of steroid inhibitors of estrone sulfatase)

IT 50-28-2, Estradiol, reactions 53-16-7, Estrone, reactions 57-63-6,  
17 $\alpha$ -Ethyneylestradiol 1530-32-1, Ethyltriphenylphosphonium bromide  
1779-51-7, Butyltriphenylphosphonium bromide 4954-12-5 6228-47-3,  
Propyltriphenylphosphonium bromide 7678-95-7 59077-04-2,  
19-Norpregna-1,3,5(10)-trien-3-ol  
RL: RCT (Reactant); RACT (Reactant or reagent)  
(preparation of steroid inhibitors of estrone sulfatase)

IT 4736-62-3P 6599-97-9P 13879-55-5P 13879-56-6P 31559-62-3P  
34111-53-0P 57711-40-7P 64215-82-3P 99898-93-8P  
120574-27-8P 120574-28-9P 123715-79-7P 137352-12-6P 206442-55-9P  
208758-18-3P 208758-19-4P 208758-24-1P 208758-26-3P 208758-27-4P  
208758-28-5P 208758-29-6P 208758-30-9P 208758-31-0P 208758-32-1P  
208758-40-1P 208758-42-3P 208758-44-5P 208758-45-6P 208758-46-7P  
208758-47-8P 208758-50-3P 208758-51-4P 208758-53-6P  
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
(preparation of steroid inhibitors of estrone sulfatase)

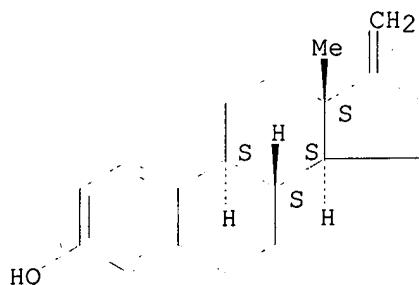
IT 208758-49-0P  
RL: SPN (Synthetic preparation); PREP (Preparation)  
(preparation of steroid inhibitors of estrone sulfatase)

RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD  
RE  
(1) Babcock; US 4297350 1981 HCPLUS  
(2) Kuehne; US 3033860 1962 HCPLUS

IT 34111-53-0P  
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
(preparation of steroid inhibitors of estrone sulfatase)

RN 34111-53-0 HCPLUS  
CN Estra-1,3,5(10)-trien-3-ol, 17-methylene- (7CI, 8CI, 9CI) (CA INDEX NAME)

Absolute stereochemistry.



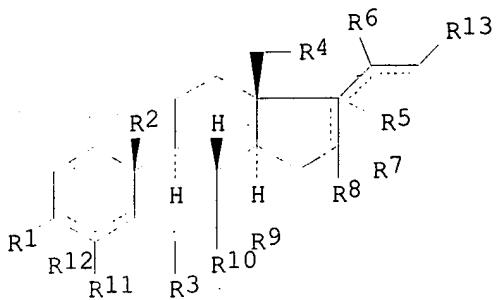
L89 ANSWER 8 OF 22 HCAPLUS COPYRIGHT 2003 ACS on STN  
 AN 1998:219719 HCAPLUS  
 DN 128:294938  
 ED Entered STN: 18 Apr 1998  
 TI Preparation of steroids as neurochemical stimulators of the vomeronasal organ (VNO) to alleviate symptoms of anxiety  
 IN Jennings-White, Clive L.; Berliner, David L.; Adams, Nathan W.;  
 Monti-Bloch, Luis  
 PA Pherin Pharmaceuticals, USA  
 SO PCT Int. Appl., 540 pp.  
 CODEN: PIXXD2  
 DT Patent  
 LA English  
 IC ICM A61K031-56  
 CC 32-5 (Steroids)

Section cross-reference(s): 1, 2, 63

FAN.CNT 12

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9814194	A1	19980409	WO 1997-US18086	19971006 <--
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	US 6117860	A	20000912	US 1997-899094	19970723 <--
	AU 9748103	A1	19980424	AU 1997-48103	19971006 <--
PRAI	US 1996-725862	A	19961004	<--	
	US 1997-899094	A	19970723	<--	
	US 1994-286073	A2	19940804	<--	
	US 1996-625268	A2	19960329	<--	
	US 1996-686092	A2	19960723	<--	
	WO 1997-US18086	W	19971006	<--	

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AB Steroids, such as I [R1 = oxo, OH, alkoxy; R2 = alkyl, etc.; R3 = H, oxo, halo, OH, etc.; R4 - R12 = H, Me, etc.; R13 = H, Me, methylene, etc.; R2R3 = cyclic ether], were prepared for nasal administration to alleviate symptoms of anxiety. The nasally administered steroid, which is a human vomeropherin, binds to a specific neuroepithelial receptor. Thus,  $3\alpha$ - and  $3\beta$ -pregna-4,20-dien-3-ols were prepared in 14 and 23% yields, resp., by reduction of pregnna-4,20-dien-3-one using lithium trisamylborohydride in THF. Autonomic responses to stimulation of the VNO by the prepared compds. was measured.

ST steroid prepn neurochem stimulator vomeronasal organ

IT Drug delivery systems

(nasal; preparation of steroids as neurochem. stimulators of the vomeronasal organ (VNO) to alleviate symptoms of anxiety)

IT Neurohormone receptors

RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)

(neuroepithelial; preparation of steroids as neurochem. stimulators of the vomeronasal organ (VNO) to alleviate symptoms of anxiety)

IT Anxiolytics

(preparation of steroids as neurochem. stimulators of the vomeronasal organ (VNO) to alleviate symptoms of anxiety)

IT Nose

(vomeronasal organ; preparation of steroids as neurochem. stimulators of the vomeronasal organ (VNO) to alleviate symptoms of anxiety)

IT 846-45-7P 1150-90-9P, Estra-1,3,5(10),16-tetraen-3-ol 1224-94-8P

2118-31-2P 4075-07-4P, Androsta-4,16-dien-3-one 7628-02-6P

19865-18-0P 21321-88-0P 28336-31-4P 34111-53-0P

35456-72-5P 35581-65-8P, Pregna-4,16-dien-3-one 55105-93-6P

65754-63-4P, Pregna-1,4,20-trien-3-one 71496-98-5P, Estra-4,16-dien-3-one 71683-67-5P 77257-06-8P 86306-95-8P 97560-70-8P,

19-Norpregna-1,3,5(10),20-tetraen-3-ol 99898-93-8P, 19-Norpregna-1,3,5(10),17(20),20-pentaen-3-ol 105644-55-1P 105663-60-3P

161061-73-0P 161061-86-5P 161061-95-6P 161061-97-8P 161061-98-9P, Estra-5(10),16-dien-3-one 161062-00-6P 177349-45-0P 177349-47-2P

177349-58-5P, 24-Norchola-4,22-dien-3-one 177349-64-3P 177349-66-5P

177565-58-1P 177794-25-1P 177794-27-3P 177794-29-5P 177794-30-8P

177856-06-3P 177856-09-6P 177856-10-9P, Estra-1,3,5(10),7,16-pentaen-3-ol 177856-12-1P 177856-13-2P, Estra-1,3,5,7,9,16-hexaen-3-ol

177856-15-4P 177856-17-6P 177856-18-7P 178688-50-1P 178688-52-3P

186183-19-7P, 19-Norpregna-5(10),20-dien-3-one 186183-25-5P

200511-32-6P 200511-37-1P 200511-39-3P 200511-50-8P,

19,21-Dinorchola-5(10),16-dien-3-one 202718-11-4P 205994-17-8P

205994-18-9P 205994-19-0P 205994-25-8P, Androsta-3,5,16-trien-3-ol

205994-26-9P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

(preparation of steroids as neurochem. stimulators of the vomeronasal organ (VNO) to alleviate symptoms of anxiety)

IT 472-56-0P 3091-04-1P, Pregna-5,17,20-dien-3 $\beta$ -ol 4350-65-6P  
 14508-15-7P, Pregna-4,20-dien-3-one 16377-13-2P 21321-95-9P  
 23062-06-8P 26400-72-6P 30505-67-0P 58594-49-3P 63014-91-5P,  
 Androsta-4,6,16-trien-3-one 71016-68-7P 86306-63-0P 86306-96-9P  
 99898-92-7P, 19-Norpregna-1,3,5(10)-trien-20-yn-3-ol 161061-71-8P  
 161061-72-9P 161061-81-0P 161061-82-1P 161061-99-0P,  
 Estra-4,9,16-trien-3-one 161062-01-7P 161062-02-8P 161062-04-0P,  
 Estra-1,3,5(10),7-tetraen-3-ol 161062-05-1P 161062-09-5P  
 177349-46-1P 177349-48-3P, 24-Norchola-4,20(22)-dien-3,6-dione  
 177349-49-4P, 24-Norchola-4,20(22)-dien-3-one 177349-54-1P  
 177349-55-2P 177349-56-3P, Pregna-4,16-diene-3,6-dione 177349-57-4P,  
 Pregna-4,17(20),20-triene-3,6-dione 177349-59-6P 177349-60-9P,  
 24-Norchola-4,22-diene-3,6-dione 177349-61-0P 177349-63-2P  
 177349-65-4P 177349-67-6P 177349-68-7P 177349-69-8P 177349-72-3P,  
 Pregna-1,4,20-trien-3-ol 177349-73-4P, Pregna-4,20-diene-3,6-dione  
 177695-29-3P 177794-21-7P 177794-22-8P 177794-24-0P 177794-26-2P  
 177794-31-9P 177856-07-4P, Estra-1,3,5(10),6,16-pentaen-3-ol  
 177856-08-5P 177856-11-0P 177856-14-3P 177856-16-5P 177856-19-8P  
 177856-20-1P 177856-21-2P 177856-22-3P 177856-23-4P 178033-52-8P,  
 Estra-1,3,5(10),16-tetraene-3,6-diol 178033-53-9P, Estra-4,16-dien-3-ol  
 186183-17-5P 186183-18-6P, 19-Norpregna-1,3,5(10),16,20-pentaen-3-ol  
 186183-20-0P, 19-Norpregna-5(10),20-dien-3-ol 186183-21-1P  
 186183-22-2P, 19-Norpregna-4,9,20-trien-3-one 186183-26-6P  
 190596-13-5P, Estra-5(10),16-dien-3-ol 200511-34-8P 200574-68-1P,  
 19,21-Dinorchol-4-en-3-one 202718-04-5P 202718-08-9P 202718-10-3P  
 205994-20-3P 205994-21-4P 205994-22-5P 205994-23-6P 205994-27-0P  
 205994-28-1P 205994-29-2P 205994-34-9P 205994-66-7P 205994-68-9P,  
 Pregna-1,5,20-trien-3-one 205994-73-6P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of steroids as neurochem. stimulators of the vomeronasal organ (VNO) to alleviate symptoms of anxiety)

IT 53-16-7, Estrone, reactions 53-43-0 57-63-6 58-22-0, Testosterone  
 145-13-1, 3 $\beta$ -HydroxyPregn-5-en-20-one 474-86-2, Equilin 517-09-9,  
 Equilenin 1162-53-4 1425-10-1 2208-12-0, 6-Dehydroestrone  
 2857-45-6 3604-60-2 4736-62-3 13244-39-8 13258-68-9 14030-45-6  
 16397-00-5 17879-91-3 21321-89-1, Pregna-4-en-20-yn-3-one 33767-87-2  
 38388-13-5 38978-06-2 39006-59-2 57597-07-6 59452-16-3,  
 19,21-Dinorchola-1,3,5(10)-trien-3-ol 60149-52-2 60149-53-3,  
 19-Norpregna-4,20-dien-3-one 71716-18-2 93998-04-0 120574-28-9  
 161061-70-7 177349-71-2 177349-74-5 178603-56-0 205994-49-6

RL: RCT (Reactant); RACT (Reactant or reagent)

(preparation of steroids as neurochem. stimulators of the vomeronasal organ (VNO) to alleviate symptoms of anxiety)

IT 34988-34-6P 205994-39-4P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of steroids as neurochem. stimulators of the vomeronasal organ (VNO) to alleviate symptoms of anxiety)

RE.CNT 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

(1) Berliner; US 5563131 A 1996 HCPLUS

IT 34111-53-0P

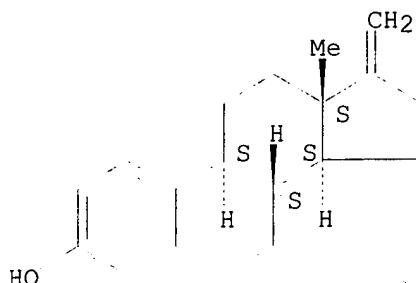
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

(preparation of steroids as neurochem. stimulators of the vomeronasal organ (VNO) to alleviate symptoms of anxiety)

RN 34111-53-0 HCPLUS

CN Estra-1,3,5(10)-trien-3-ol, 17-methylene- (7CI, 8CI, 9CI) (CA INDEX NAME)

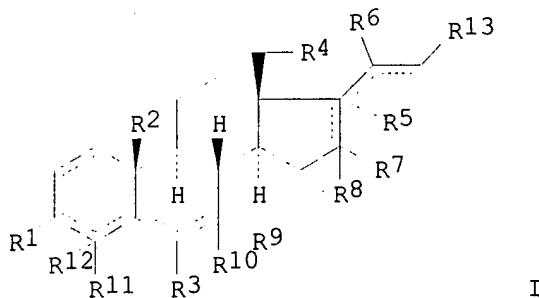
## Absolute stereochemistry.



L89 ANSWER 9 OF 22 HCPLUS COPYRIGHT 2003 ACS on STN  
AN 1998:87643 HCPLUS  
DN 128:154277  
ED Entered STN: 14 Feb 1998  
TI Preparation of steroids as neurochemical stimulators of the VNO to alleviate symptoms of PMS and anxiety  
IN Jennings-White, Clive L.; Berliner, David L.; Adams, Nathan W.; Bloch-Monti, Luis  
PA Pherin Corp., USA  
SO PCT Int. Appl., 551 pp.  
CODEN: PIXXD2  
DT Patent  
LA English  
IC ICM A61K051-04  
ICS C07J071-00  
CC 32-5 (Steroids)  
Section cross-reference(s): 2, 63

FAN.CNT 12						
	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
PI	WO 9803207	A1	19980129	WO 1997-US13035	19970723	<--
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM					
	RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG					
	US 6057439	A	20000502	US 1996-686092	19960723	<--
	AU 9739637	A1	19980210	AU 1997-39637	19970723	<--
	AU 726625	B2	20001116			
	EP 914165	A1	19990512	EP 1997-937019	19970723	<--
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO					
	BR 97111812	A	19990824	BR 1997-11812	19970723	<--
	NZ 333671	A	20000728	NZ 1997-333671	19970723	<--
	JP 2000513000	T2	20001003	JP 1998-507230	19970723	<--
	NO 9900305	A	19990322	NO 1999-305	19990122	<--
	MX 9900885	A	20000331	MX 1999-885	19990122	<--
PRAI	US 1996-686092	A	19960723	<--		
	US 1996-725862	A	19961004	<--		
	US 1994-286073	A2	19940804	<--		
	US 1996-625268	A2	19960329	<--		
	WO 1997-US13035	W	19970723	<--		
OS	MARPAT 128:154277					

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- AB Compds. such as formula I [R1 = oxo, (substituted) OH; R2 = alkyl, etc.; R3 = H, oxo, halo, OH, etc.; R4-R12 = H, halo, Me; R13 = H, Me, methylene, etc.; R2R3 = cyclic ether] are prepared. The invention relates to a method of alleviating the symptoms of PMS and anxiety. The method comprises nasally administering a steroid which is a human vomeropherin, such that the vomeropherin binds to a specific neuroepithelial receptor. The steroid or steroids is/are preferably administered in the form of a pharmaceutical composition containing one or more pharmaceutically acceptable carriers.
- ST steroid prepn neurochem stimulator vomeronasal organ
- IT Drug delivery systems  
(nasal; preparation of steroids as neurochem. stimulators of the vomeronasal organ)
- IT Receptors  
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)  
(neuroepithelial; preparation of steroids as neurochem. stimulators of the vomeronasal organ)
- IT Ovarian cycle  
(premenstrual syndrome; preparation of steroids as neurochem. stimulators of the vomeronasal organ)
- IT Anxiolytics  
(preparation of steroids as neurochem. stimulators of the vomeronasal organ)
- IT Nose  
(vomeronasal organ; preparation of steroids as neurochem. stimulators of the vomeronasal organ)
- IT 1150-90-9P, Estra-1,3,5(10),16-tetraen-3-ol 4075-07-4P,  
Androsta-4,16-dien-3-one 4736-62-3P 14508-15-7P, Pregna-4,20-dien-3-one 28336-31-4P 65754-63-4P, Pregna-1,4,20-trien-3-one 71496-98-5P,  
Estra-4,16-dien-3-one 161061-70-7P 161061-73-0P 161061-81-0P  
161061-82-1P 161061-97-8P 177349-47-2P 177349-52-9P 177349-58-5P,  
24-Norchola-4,22-dien-3-one 177856-07-4P, Estra-1,3,5(10),6,16-pentaen-3-ol 178688-52-3P 200511-50-8P, 19,21-Dinorchola-5(10),16-dien-3-one 202718-11-4P  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)  
(preparation of steroids as neurochem. stimulators of the vomeronasal organ)
- IT 53-63-4P, Estra-1,3,5(10)-trien-3-ol 472-56-0P 2872-90-4P,  
Androst-4-en-3-one 16377-13-2P 21321-95-9P 23062-06-8P 26400-72-6P  
30505-67-0P 58594-49-3P 63014-91-5P, Androsta-4,6,16-trien-3-one  
86306-63-0P 86306-96-9P 99898-92-7P, 19-Norpregna-1,3,5(10)-trien-20-yn-3-ol 114611-55-1P, Androsta-4,16-diene-3,6-dione 161061-71-8P  
161061-72-9P 161061-83-2P 161061-84-3P 161061-99-0P,  
Estra-4,9,16-trien-3-one 161062-01-7P 161062-02-8P 161062-04-0P,

Estra-1,3,5(10),7-tetraen-3-ol 161062-05-1P 161062-06-2P,  
 Estra-1,3,5(10),6-tetraen-3-ol 161062-08-4P 161062-09-5P  
 177349-46-1P 177349-48-3P, 24-Norchola-4,20(22)-diene-3,6-dione  
 177349-49-4P, 24-Norchola-4,20(22)-dien-3-one 177349-53-0P  
 177349-54-1P 177349-55-2P 177349-56-3P, Pregna-4,16-diene-3,6-dione  
 177349-57-4P, Pregna-4,17(20),20-triene-3,6-dione 177349-59-6P  
 177349-60-9P, 24-Norchola-4,22-diene-3,6-dione 177349-61-0P  
 177349-62-1P 177349-63-2P 177349-65-4P 177349-67-6P 177349-68-7P  
 177349-69-8P 177349-72-3P, Pregna-1,4,20-trien-3-ol 177349-73-4P,  
 Pregna-4,20-diene-3,6-dione 177695-29-3P 177794-21-7P 177794-22-8P  
 177794-23-9P 177794-24-0P 177794-26-2P 177794-27-3P 177794-31-9P  
 177794-32-0P 177856-05-2P 177856-08-5P 177856-11-0P 177856-14-3P  
 177856-16-5P 177856-19-8P 177856-20-1P 177856-21-2P 177856-22-3P  
 177856-23-4P 178033-52-8P, Estra-1,3,5(10),16-tetraene-3,6-diol  
 186183-53-9P, Estra-4,16-dien-3-ol 186183-17-5P 186183-18-6P  
 186183-20-0P, 19-Norpregna-5(10),20-dien-3-ol 186183-21-1P  
 186183-22-2P, 19-Norpregna-4,9,20-trien-3-one 186183-26-6P  
 186183-28-8P 186183-29-9P 200511-34-8P 200574-68-1P,  
 19,21-Dinorchol-4-en-3-one 202718-04-5P 202718-06-7P 202718-07-8P  
 202718-08-9P 202718-09-0P 202718-10-3P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of steroids as neurochem. stimulators of the vomeronasal organ)

IT 53-16-7, Estrone, reactions 53-43-0, Dehydroepiandrosterone 57-63-6,  
 Ethinylestradiol 58-22-0, Testosterone 145-13-1 434-22-0,  
 19-Nortestosterone 474-86-2, Equilin 517-09-9, Equilenin 1162-53-4  
 1434-85-1 2118-31-2 2208-12-0, 6-Dehydroestrone 2857-45-6  
 3604-60-2 13244-39-8 13258-68-9 14030-45-6 16397-00-5 17879-91-3  
 21321-88-0 21321-89-1, Pregn-4-en-20-yn-3-one 35581-65-8,  
 Pregna-4,16-dien-3-one 38388-13-5 38978-06-2 39006-59-2 57597-07-6  
 60149-52-2 60149-53-3, 19-Norpregna-4,20-dien-3-one 63015-08-7,  
 Androsta-1,4,16-trien-3-one 71716-18-2 93998-04-0 120574-28-9  
 177349-70-1 177349-71-2 177565-58-1 177794-28-4

RL: RCT (Reactant); RACT (Reactant or reagent)

(preparation of steroids as neurochem. stimulators of the vomeronasal organ)

IT 846-45-7P 1224-94-8P 7628-02-6P, Estrone hydrazone 19865-18-0P  
 33767-87-2P 34111-53-0P 34988-34-6P 35456-72-5P  
 55105-93-6P 59452-16-3P, 19,21-Dinorchola-1,3,5(10)-trien-3-ol  
 71683-67-5P 77257-06-8P 86306-95-8P 97560-70-8P,  
 19-Norpregna-1,3,5(10),20-tetraen-3-ol 99898-93-8P 103614-70-6P,  
 Androsta-5,16-dien-3-one 105644-55-1P 105663-60-3P 161061-86-5P  
 161061-93-4P 161061-95-6P 161061-98-9P, Estra-5(10),16-dien-3-one  
 161062-00-6P 177349-45-0P 177349-50-7P 177349-51-8P 177349-64-3P  
 177349-66-5P 177349-74-5P 177794-25-1P 177794-29-5P 177794-30-8P  
 177856-06-3P 177856-09-6P 177856-10-9P, Estra-1,3,5(10),7,16-pentaen-3-  
 ol 177856-12-1P 177856-13-2P, Estra-1,3,5,7,9,16-hexaen-3-ol  
 177856-15-4P 177856-17-6P 177856-18-7P 178688-50-1P 186183-19-7P,  
 19-Norpregna-5(10),20-dien-3-one 186183-25-5P 200511-32-6P  
 200511-37-1P 200511-39-3P 202718-05-6P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of steroids as neurochem. stimulators of the vomeronasal organ)

RE.CNT 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

(1) Gee; US 5208227 1993 HCPLUS

IT 34111-53-0P

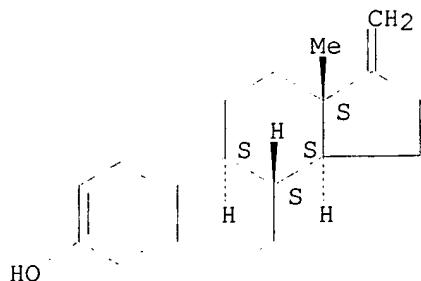
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of steroids as neurochem. stimulators of the vomeronasal organ)

RN 34111-53-0 HCPLUS

CN Estra-1,3,5(10)-trien-3-ol, 17-methylene- (7CI, 8CI, 9CI) (CA INDEX NAME)

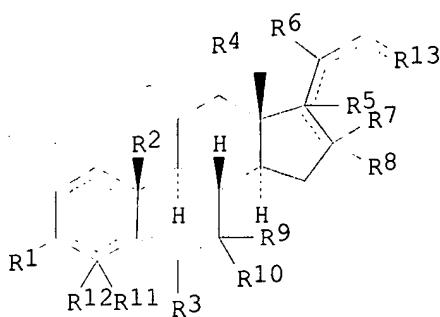
Absolute stereochemistry.



L89 ANSWER 10 OF 22 HCAPLUS COPYRIGHT 2003 ACS on STN  
 AN 1997:672282 HCAPLUS  
 DN 127:293468  
 ED Entered STN: 23 Oct 1997  
 TI Preparation of steroids as neurochemical initiators of change in human blood levels of LH or FSH  
 IN Jennings-White, Clive L.; Berliner, David L.; Adams, Nathan W.  
 PA Pherin Corp., USA  
 SO PCT Int. Appl., 498 pp.  
 CODEN: PIXXD2  
 DT Patent  
 LA English  
 IC ICM A61K031-56  
 CC 32-5 (Steroids)  
 Section cross-reference(s): 2, 63  
 FAN.CNT 12

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9736596	A1	19971009	WO 1997-US6061	19970328 <--
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	US 6066627	A	20000523	US 1996-625268	19960329 <--
	AU 9726650	A1	19971022	AU 1997-26650	19970328 <--
	AU 735804	B2	20010712		
	EP 891188	A1	19990120	EP 1997-918578	19970328 <--
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
	BR 9708399	A	19990803	BR 1997-8399	19970328 <--
	JP 2000504025	T2	20000404	JP 1997-535629	19970328 <--
PRAI	US 1996-625268	A	19960329 <--		
	US 1994-286073	A2	19940804 <--		
	WO 1997-US6061	W	19970328 <--		

GI



- AB** The invention relates to a method of altering the blood levels of LH or FSH in an individual. Steroids of formula I [R1 = oxo, OH, OAc, O<sub>2</sub>CET, methoxy, etc.; R2 = Me, HOCH<sub>2</sub>, acyloxymethyl, alkyl, etc.; R3 = H, oxo, halo, OH, alkoxy, acyloxy; R4-R12 = H, halo, Me, halomethyl; R13 = H, Me, methylene, Et, ethenyl, acetylenyl, etc.], and others are prepared. The method comprises nasally administering a steroid which is a human vomeropherin, such that the vomeropherin binds to a specific neuroepithelial receptor. The steroid or steroids is/are preferably administered in the form of a pharmaceutical composition containing one or more pharmaceutically acceptable carriers. Thus, 1,3,5(10),16-estratetraen-3-ol is prepared from estrone via hydrazone formation and reduction. 1,3,5(10),16-Estratetraen-3-ol is shown to have autonomic activity.
- ST** FSH regulation steroid prepn; testosterone regulation steroid prepn; vomeronasal organ FSH regulation steroid prepn; neuroepithelial receptor FSH regulation steroid prepn; LH regulation steroid prepn
- IT** Drug delivery systems  
(nasal; preparation of steroids as neurochem. initiators of change in human blood levels of LH or FSH)
- IT** Receptors  
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)  
(neuroepithelial; preparation of steroids as neurochem. initiators of change in human blood levels of LH or FSH)
- IT** Nose  
(neuroepithelium; preparation of steroids as neurochem. initiators of change in human blood levels of LH or FSH)
- IT** Nose  
(vomeronasal organ; preparation of steroids as neurochem. initiators of change in human blood levels of LH or FSH)
- IT** 28336-31-4P  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent)  
(preparation of steroids as neurochem. initiators of change in human blood levels of LH or FSH)
- IT** 1150-90-9P, Estra-1,3,5(10),16-tetraen-3-ol 4075-07-4P,  
Androsta-4,16-dien-3-one 65754-63-4P, Pregna-1,4,20-trien-3-one  
161061-73-0P 177349-45-0P 177349-47-2P 177349-52-9P 177349-74-5P  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)  
(preparation of steroids as neurochem. initiators of change in human blood levels of LH or FSH)
- IT** 2118-31-2  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); THU (Therapeutic use); BIOL (Biological study); RACT (Reactant or reagent); USES (Uses)

- (preparation of steroids as neurochem. initiators of change in human blood levels of LH or FSH)
- IT 53-63-4P, Estra-1,3,5(10)-trien-3-ol 2872-90-4P, Androst-4-en-3-one  
 21321-95-9P 23062-06-8P 26400-72-6P 30505-67-0P 58594-49-3P  
 63014-91-5P, Androsta-4,6,16-trien-3-one 86306-63-0P 86306-96-9P  
 114611-55-1P, Androsta-4,16-diene-3,6-dione 120476-05-3P 161061-71-8P  
 161061-72-9P 161061-81-0P 161061-82-1P 161061-83-2P 161061-84-3P  
 161061-99-0P, Estra-4,9,16-trien-3-one 161062-01-7P 161062-02-8P  
 161062-04-0P, Estra-1,3,5(10),7-tetraen-3-ol 161062-05-1P  
 161062-06-2P, Estra-1,3,5(10),6-tetraen-3-ol 161062-08-4P 161062-09-5P  
 177349-46-1P 177349-48-3P, 24-Norchola-4,20(22)-dien-3,6-dione  
 177349-49-4P, 24-Norchola-4,20(22)-dien-3-one 177349-53-0P  
 177349-54-1P 177349-55-2P 177349-56-3P, Pregna-4,16-diene-3,6-dione  
 177349-57-4P, Pregna-4,17(20),20-triene-3,6-dione 177349-59-6P  
 177349-60-9P, 24-Norchola-4,22-diene-3,6-dione 177349-61-0P  
 177349-62-1P 177349-63-2P 177349-65-4P 177349-67-6P 177349-68-7P  
 177349-69-8P 177349-72-3P, Pregna-1,4,20-trien-3-ol 177349-73-4P,  
 Pregna-4,20-diene-3,6-dione 177695-29-3P 177794-21-7P 177794-22-8P  
 177794-23-9P 177794-24-0P 177794-26-2P 177794-27-3P 177794-31-9P  
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 177856-16-5P 177856-19-8P 177856-20-1P 177856-21-2P 177856-22-3P  
 177856-23-4P 178033-52-8P, Estra-1,3,5(10),16-tetraene-3,6-diol  
 178033-53-9P, Estra-4,16-dien-3-ol 186183-17-5P 186183-18-6P  
 186183-20-0P, 19-Norpregna-5(10),20-dien-3-ol 186183-21-1P  
 186183-22-2P, 19-Norpregna-4,9,20-trien-3-one 186183-26-6P  
 186183-27-7P 186183-28-8P 186183-29-9P 197094-33-0P 197094-34-1P  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use);  
 BIOL (Biological study); PREP (Preparation); USES (Uses)  
 (preparation of steroids as neurochem. initiators of change in human blood levels of LH or FSH)
- IT 9002-67-9, Luteinizing hormone 9002-68-0, Follicle stimulating hormone  
 RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)  
 (preparation of steroids as neurochem. initiators of change in human blood levels of LH or FSH)
- IT 58-22-0, Testosterone  
 RL: BPR (Biological process); BSU (Biological study, unclassified); RCT (Reactant); BIOL (Biological study); PROC (Process); RACT (Reactant or reagent)  
 (preparation of steroids as neurochem. initiators of change in human blood levels of LH or FSH)
- IT 53-16-7, Estrone, reactions 53-43-0, Dehydroepiandrosterone 57-63-6  
 145-13-1 434-22-0, 19-Nortestosterone 474-86-2, Equilin 517-09-9,  
 Equilenin 1162-53-4 2208-12-0, 6-Dehydroestrone 2857-45-6  
 3604-60-2 6228-47-3, Propyltriphenylphosphonium bromide 13244-39-8  
 13258-68-9 14030-45-6 14508-15-7, Pregna-4,20-dien-3-one 17879-91-3  
 21321-88-0, Pregna-5,20-dien-3 $\beta$ -ol 21321-89-1, Pregn-4-en-20-yn-3-one 38388-13-5 38978-06-2 39006-59-2 57597-07-6 60149-52-2  
 60149-53-3, 19-Norpregna-4,20-dien-3-one 63015-08-7,  
 Androsta-1,4,16-trien-3-one 71716-18-2 93998-04-0 177349-70-1  
 177349-71-2 177565-58-1 177794-28-4 178603-56-0 190596-19-1  
 RL: RCT (Reactant); RACT (Reactant or reagent)  
 (preparation of steroids as neurochem. initiators of change in human blood levels of LH or FSH)
- IT 846-45-7P 1224-94-8P 19865-18-0P 34111-53-0P 34988-34-6P  
 35456-72-5P 55105-93-6P 71496-98-5P, Estra-4,16-dien-3-one  
 77257-06-8P 86306-95-8P 97560-70-8P, 19-Norpregna-1,3,5(10),20-tetraen-3-ol 99898-92-7P, 19-Norpregna-1,3,5(10)-trien-20-yn-3-ol 99898-93-8P  
 103614-70-6P, Androsta-5,16-dien-3-one 161061-70-7P 161061-86-5P  
 161061-93-4P 161061-95-6P 161061-97-8P 161061-98-9P,  
 Estra-5(10),16-dien-3-one 161062-00-6P 177349-50-7P 177349-51-8P  
 177349-58-5P, 24-Norchola-4,22-dien-3-one 177349-64-3P 177349-66-5P

177794-25-1P 177794-29-5P 177794-30-8P 177856-06-3P 177856-07-4P,  
 Estra-1,3,5(10),6,16-pentaen-3-ol 177856-09-6P 177856-10-9P,  
 Estra-1,3,5(10),7,16-pentaen-3-ol 177856-12-1P 177856-13-2P,  
 Estra-1,3,5,7,9,16-hexaen-3-ol 177856-15-4P 177856-17-6P  
 177856-18-7P 186183-19-7P, 19-Norpregna-5(10),20-dien-3-one  
 186183-25-5P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT  
 (Reactant or reagent)  
 (preparation of steroids as neurochem. initiators of change in human blood  
 levels of LH or FSH)

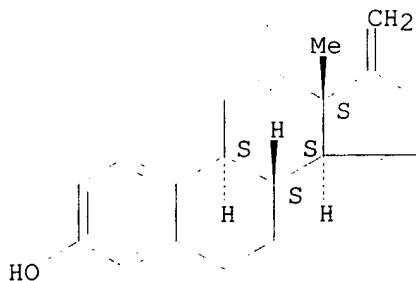
IT 34111-53-0P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT  
 (Reactant or reagent)  
 (preparation of steroids as neurochem. initiators of change in human blood  
 levels of LH or FSH)

RN 34111-53-0 HCPLUS

CN Estra-1,3,5(10)-trien-3-ol, 17-methylene- (7CI, 8CI, 9CI) (CA INDEX NAME)

Absolute stereochemistry.



L89 ANSWER 11 OF 22 HCPLUS COPYRIGHT 2003 ACS on STN

AN 1997:394816 HCPLUS

DN 127:17859

ED Entered STN: 26 Jun 1997

TI Preparation of estrenes for inducing hypothalamic effects

IN Berliner, David L.; Adams, Nathan W.; Jennings-White, Clive L.

PA Pherin Corporation, USA

SO U.S., 63 pp., Division of U.S. Ser. No. 316,050.

CODEN: USXXAM

DT Patent

LA English

IC ICM C07J013-00

NCL 552530000

CC 32-3 (Steroids)

Section cross-reference(s): 1

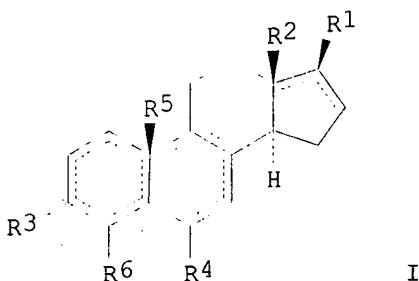
FAN.CNT 7

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 5633392	A	19970527	US 1995-454917	19950531 <--
	US 5783571	A	19980721	US 1993-127980	19930928 <--
	NZ 333837	A	20000526	NZ 1995-333837	19950529 <--
	EP 924219	A2	19990623	EP 1998-203950	19950929 <--
	EP 924219	A3	20020123		
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	US 2002143001	A1	20021003	US 2001-922216	20010803 <--
PRAI	US 1991-638743	B2	19910107	<--	
	US 1991-707862	B2	19910531	<--	
	US 1992-903525	B2	19920624	<--	
	US 1993-127980	A2	19930928	<--	

US 1994-316050	A3	19940929	<--
US 1993-127908	B2	19930928	<--
EP 1995-935237	A3	19950929	<--
NZ 1995-294510	A1	19950929	<--
US 1996-654021	A1	19960528	<--
US 1999-249462	B1	19990212	<--

OS MARPAT 127:17859

GI



AB The invention relates to estrene steroids, which bind to neuroepithelial receptors. Title compds. I [R1 = CH<sub>2</sub>, Me; R2 = null, H, Me; R3 = oxo, OH, alkoxy, acyloxy, benzoyl, etc.; R4 = H, OH, alkoxy, acyloxy, oxo, halo; R5 = null, H, OH, alkoxy, acyloxy; R6 = H, halo; with provisos] are prepared and tested for their effect on olfactory receptors. Refluxing a mixture of estrone, p-toluenesulfonylhydrazide in methanol for 20 h gave estrone p-toluenesulfonylhydrazone, which was treated with BuLi in hexane-THF with ice cooling to give the title compound estra-1,3,5(10),16-tetraen-3-ol. Stimulation on human vomeronasal organ by this gave a local elec. potential response of ca. 22 mV-seconds vs. ca. 8 mV-seconds for androstadien-3-one.

ST estrene prepn hypothalamic effect

IT Brain

(hypothalamus; preparation of estrenes for inducing hypothalamic effects)

IT Drug delivery systems

(nasal; preparation of estrenes for inducing hypothalamic effects)

IT Anxiolytics

Odor and Odorous substances

(preparation of estrenes for inducing hypothalamic effects)

IT Steroids, preparation

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of estrenes for inducing hypothalamic effects)

IT Sensory receptors

RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)

(preparation of estrenes for inducing hypothalamic effects)

IT 1150-90-9P, Estra-1,3,5(10),16-tetraen-3-ol 34111-53-0P

35456-72-5P 71496-98-5P, Estra-4,16-dien-3-one 77257-06-8P

161061-73-0P 161061-97-8P 161061-98-9P, Estra-5(10),16-dien-3-one

161062-00-6P 161062-01-7P 161167-82-4P, Estr-16-en-3-one

177856-06-3P 177856-09-6P 177856-10-9P, Estra-1,3,5(10),7,16-pentaen-3-ol 177856-13-2P, Estra-1,3,5,7,9,16-hexaen-3-ol 177856-15-4P

177856-17-6P 177856-18-7P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT

(Reactant or reagent); USES (Uses)  
 (preparation of estrenes for inducing hypothalamic effects)

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 Estra-1,3,5(10),7-tetraen-3-ol 161062-05-1P 161062-06-2P,  
 Estra-1,3,5(10),6-tetraen-3-ol 177856-07-4P, Estra-1,3,5(10),6,16-  
 pentaen-3-ol 177856-08-5P 177856-11-0P 177856-12-1P 177856-14-3P  
 177856-16-5P 177856-19-8P 177856-20-1P 177856-21-2P 177856-22-3P  
 177856-23-4P 178033-52-8P, Estra-1,3,5(10),16-tetraene-3,6-diol  
 178033-53-9P, Estra-4,16-dien-3-ol 190596-13-5P, Estra-5(10),16-dien-3-  
 ol 190596-16-8P 190596-17-9P 190596-18-0P, Estra-4,8,16-trien-3-one  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological  
 study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use);  
 BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of estrenes for inducing hypothalamic effects)

IT 53-16-7, Estrone, reactions 434-22-0, 19-Nortestosterone 474-86-2,  
 Equilin 517-09-9, Equilenin 1576-35-8, p-Toluenesulfonylhydrazide  
 1779-49-3, Triphenylmethylphosphonium bromide 2208-12-0,  
 6-Dehydroestrone 28336-31-4 93998-04-0 190596-19-1  
 RL: RCT (Reactant); RACT (Reactant or reagent)

(preparation of estrenes for inducing hypothalamic effects)

IT 1425-10-1P, 19-Nortestosterone acetate 55105-93-6P  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT  
 (Reactant or reagent)

(preparation of estrenes for inducing hypothalamic effects)

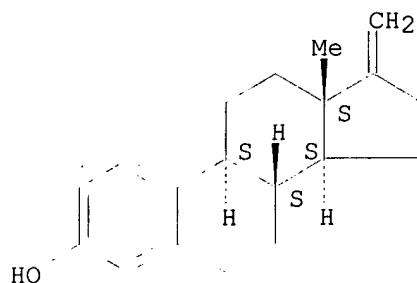
IT 34111-53-0P  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological  
 study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU  
 (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT  
 (Reactant or reagent); USES (Uses)

(preparation of estrenes for inducing hypothalamic effects)

RN 34111-53-0 HCPLUS

CN Estra-1,3,5(10)-trien-3-ol, 17-methylene- (7CI, 8CI, 9CI) (CA INDEX NAME)

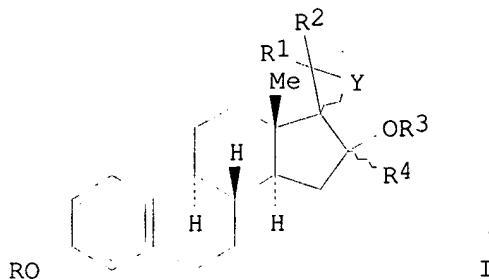
Absolute stereochemistry.



L89 ANSWER 12 OF 22 HCPLUS COPYRIGHT 2003 ACS on STN  
 AN 1997:244398 HCPLUS  
 DN 126:225448  
 ED Entered STN: 16 Apr 1997  
 TI Novel estrogens for treating autoimmune diseases  
 IN Brattsand, Ralph; Holmdahl, Rikard; Jansson, Liselotte; Loncar, Marjana;  
 Pettersson, Lars  
 PA Astra Aktiebolag, Swed.; Brattsand, Ralph; Holmdahl, Rikard; Jansson,  
 Liselotte; Loncar, Marjana; Pettersson, Lars  
 SO PCT Int. Appl., 53 pp.  
 CODEN: PIXXD2  
 DT Patent  
 LA English  
 IC ICM C07J053-00  
 CC 32-3 (Steroids)

## FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9708188	A1	19970306	WO 1996-SE1028	19960820 <--
	W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM				
	CA 2228803	AA	19970306	CA 1996-2228803	19960820 <--
	AU 9668405	A1	19970319	AU 1996-68405	19960820 <--
	EP 847399	A1	19980617	EP 1996-928771	19960820 <--
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI				
	JP 11511457	T2	19991005	JP 1997-510174	19960820 <--
	US 6043236	A	20000328	US 1997-817683	19970423 <--
PRAI	SE 1995-2921	A	19950823	<--	
	WO 1996-SE1028	W	19960820	<--	
OS	MARPAT	126:225448			
GI					



AB Estratrienes I [R = H, alkyl, cycloalkyl, acyl, alkoxy carbonyl, aralkoxy carbonyl, protective group; R<sub>1</sub>, R<sub>2</sub> = H, Me, Et, halogen; R<sub>3</sub> = H, acyl, alkoxy carbonyl, aralkoxy carbonyl; R<sub>4</sub> = H, Me, Et; Y = CH<sub>2</sub>, bond] were prepared. Thus, estrone was converted to its 3-dimethylhexyl ether which was treated with Et<sub>3</sub>PPH<sub>3</sub>+ Br-, followed by SeO<sub>2</sub>-Me<sub>3</sub>COOH oxidation and desilylation to give (17E)-3,16 $\alpha$ -dihydroxy-19-norpregna-1,3,5(10),17(20)-tetraene. It shows very low sex hormone side effects while retaining their antiinflammatory and immunosuppressant activity.

ST estratriene deriv prepn antiinflammatory immunosuppressant

IT Anti-inflammatory agents

Immunosuppressants

(preparation of estratriene derivs. as inflammation inhibitors and immunosuppressants)

IT Estrogens

RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of estratriene derivs. as inflammation inhibitors and immunosuppressants)

IT 50-27-1, Estradiol 53-16-7, Estrone, reactions 867-13-0, Triethyl phosphonoacetate 34111-53-0

RL: RCT (Reactant); RACT (Reactant or reagent)

(preparation of estratriene derivs. as inflammation inhibitors and immunosuppressants)

IT 188291-18-1P 188291-19-2P 188291-20-5P 188291-21-6P 188291-22-7P

188291-23-8P 188291-27-2P 188291-30-7P 188291-31-8P 188291-33-0P  
 188291-34-1P 188291-36-3P 188291-37-4P 188291-38-5P 188291-39-6P  
 188291-42-1P 188291-43-2P 188291-44-3P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of estratriene derivs. as inflammation inhibitors and immunosuppressants)

IT 70574-32-2P 188291-24-9P 188291-25-0P 188291-26-1P 188291-28-3P  
 188291-29-4P 188291-32-9P 188291-35-2P 188291-40-9P 188291-41-0P  
 188291-45-4P 188291-48-7P 188291-49-8P 188291-50-1P 188291-51-2P  
 188291-52-3P 188291-53-4P 188291-54-5P 188291-55-6P 188291-56-7P  
 188291-57-8P 188291-58-9P 188291-60-3P 188291-62-5P 188291-63-6P  
 188291-65-8P 188291-67-0P 188291-70-5P 188291-72-7P 188291-74-9P  
 188291-76-1P 188291-79-4P 188291-80-7P 188291-81-8P 188291-83-0P  
 188291-86-3P

RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of estratriene derivs. as inflammation inhibitors and immunosuppressants)

IT 34111-53-0

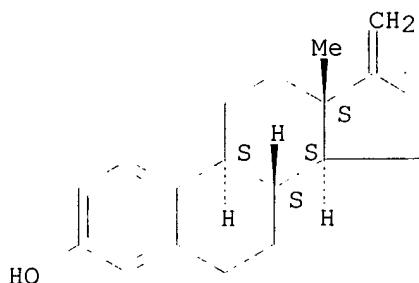
RL: RCT (Reactant); RACT (Reactant or reagent)

(preparation of estratriene derivs. as inflammation inhibitors and immunosuppressants)

RN 34111-53-0 HCPLUS

CN Estra-1,3,5(10)-trien-3-ol, 17-methylene- (7CI, 8CI, 9CI) (CA INDEX NAME)

Absolute stereochemistry.



L89 ANSWER 13 OF 22 HCPLUS COPYRIGHT 2003 ACS on STN

AN 1996:369795 HCPLUS

DN 125:58846

ED Entered STN: 27 Jun 1996

TI Novel estrenes for inducing hypothalamic effects

IN Berliner, David L.; Adams, Nathan W.; Jennings-White, Clive L.

PA Pherin Corporation, USA

SO PCT Int. Appl., 137 pp.

CODEN: PIXXD2

DT Patent

LA English

IC ICM C07J001-00

ICS C07J003-00; C07J031-00; C07J053-00

CC 32-3 (Steroids)

Section cross-reference(s): 1

FAN.CNT 7

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9610032	A1	19960404	WO 1995-US12542	19950929 <-- W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ,

TM, TT

RW: KE, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT,  
 LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE,  
 SN, TD, TG

NZ 333837	A	20000526	NZ 1995-333837	19950529 <--
CA 2199044	AA	19960404	CA 1995-2199044	19950929 <--
AU 9537331	A1	19960419	AU 1995-37331	19950929 <--
AU 705422	B2	19990520		
EP 783513	A1	19970716	EP 1995-935237	19950929 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE, IE, SI, LT, LV				
CN 1167489	A	19971210	CN 1995-196518	19950929 <--
HU 76856	A2	19971229	HU 1997-1508	19950929 <--
BR 9509098	A	19980714	BR 1995-9098	19950929 <--
JP 10509423	T2	19980914	JP 1995-512067	19950929 <--
EP 924219	A2	19990623	EP 1998-203950	19950929 <--
EP 924219	A3	20020123		

PRAI US 1994-316050 A 19940929 <--  
 EP 1995-935237 A3 19950929 <--  
 NZ 1995-294510 A1 19950929 <--  
 WO 1995-US12542 W 19950929 <--

OS MARPAT 125:58846

AB The invention relates to estrene steroid, which bind to neuroepithelial receptors. Thus, estrone is converted to its tosylhydrazone which is subjected to elimination reaction to give 1,3,5(10),16-estratetraen-3-ol (I). I elicits a response in the vomeronasal organ that is stronger in males than females.

ST estrene deriv prepn hypothalamus

IT Hypothalamus  
 (preparation of estrenes for inducing hypothalamic effects)

IT Steroids, preparation

RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
 (preparation of estrenes for inducing hypothalamic effects)

IT 28336-31-4

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); BIOL (Biological study); RACT (Reactant or reagent)  
 (preparation of estrenes for inducing hypothalamic effects)

IT 1150-90-9P, Estra-1,3,5(10),16-tetraen-3-ol 161061-73-0P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent)  
 (preparation of estrenes for inducing hypothalamic effects)

IT 161062-09-5P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)  
 (preparation of estrenes for inducing hypothalamic effects)

IT 50-27-1 58-22-0 1224-94-8 4075-07-4, Androsta-4,16-dien-3-one  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (preparation of estrenes for inducing hypothalamic effects)

IT 53-16-7, Estrone, reactions 434-22-0, 19-Nortestosterone 474-86-2,  
 Equilin 517-09-9, Equilenin 2208-12-0, 6-Dehydroestrone 33767-87-2  
 93998-04-0 161061-98-9, Estra-5(10),16-dien-3-one  
 RL: RCT (Reactant); RACT (Reactant or reagent)  
 (preparation of estrenes for inducing hypothalamic effects)

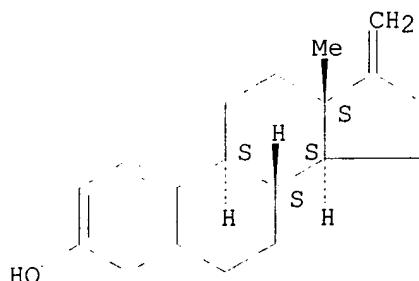
IT 34111-53-0P 35456-72-5P 55105-93-6P 71496-98-5P,  
 Estra-4,16-dien-3-one 77257-06-8P 86306-95-8P 161061-97-8P  
 161062-00-6P 177856-06-3P 177856-07-4P, Estra-1,3,5(10),6,16-pentaen-3-  
 ol 177856-09-6P 177856-10-9P, Estra-1,3,5(10),7,16-pentaen-3-ol  
 177856-12-1P 177856-15-4P 177856-17-6P 177856-18-7P  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT  
 (Reactant or reagent)  
 (preparation of estrenes for inducing hypothalamic effects)

IT 58594-49-3P 86306-96-9P 161061-99-0P, Estra-4,9,16-trien-3-one  
 161062-01-7P 161062-02-8P 161062-03-9P 161062-04-0P,  
 Estra-1,3,5(10),7-tetraen-3-ol 161062-05-1P 161062-06-2P,  
 Estra-1,3,5(10),6-tetraen-3-ol 161062-07-3P 161062-08-4P  
 177856-05-2P 177856-08-5P 177856-11-0P 177856-13-2P,  
 Estra-1,3,5,7,9,16-hexaen-3-ol 177856-14-3P 177856-16-5P  
 177856-19-8P 177856-20-1P 177856-21-2P 177856-22-3P 177856-23-4P  
 177856-24-5P 178033-52-8P, Estra-1,3,5(10),16-tetraene-3,6-diol  
 178033-53-9P, Estra-4,16-dien-3-ol  
 RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological  
 study); PREP (Preparation); USES (Uses)  
 (preparation of estrenes for inducing hypothalamic effects)

IT 34111-53-0P  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT  
 (Reactant or reagent)  
 (preparation of estrenes for inducing hypothalamic effects)

RN 34111-53-0 HCAPLUS  
 CN Estra-1,3,5(10)-trien-3-ol, 17-methylene- (7CI, 8CI, 9CI) (CA INDEX NAME)

Absolute stereochemistry.



L89 ANSWER 14 OF 22 HCAPLUS COPYRIGHT 2003 ACS on STN  
 AN 1992:626505 HCAPLUS  
 DN 117:226505  
 ED Entered STN: 13 Dec 1992  
 TI Synthesis and characterization of estrogen 2,3- and 3,4-quinones.  
 Comparison of DNA adducts formed by the quinones versus horseradish peroxidase-activated catechol estrogens  
 AU Dwivedy, I.; Devanesan, P.; Cremonesi, P.; Rogan, E.; Cavalieri, E.  
 CS Med. Cent., Univ. Nebraska, Omaha, NE, 68198-6805, USA  
 SO Chemical Research in Toxicology (1992), 5(6), 828-33  
 CODEN: CRTOEC; ISSN: 0893-228X  
 DT Journal  
 LA English  
 CC 2-4 (Mammalian Hormones)  
 Section cross-reference(s): 32  
 AB Catechol estrogens (CE) are among the major metabolites of estrone (E1) and 17 $\beta$ -estradiol (E2). Oxidation of these metabolites to semiquinones and quinones could generate ultimate carcinogenic forms of E1 and E2. The 2,3- and 3,4-quinones of E1 and E2 were synthesized by MnO<sub>2</sub> oxidation of the corresponding CE. Characterization of these compds. was accomplished by UV, NMR, and mass spectrometry. The relative stability of these compds.

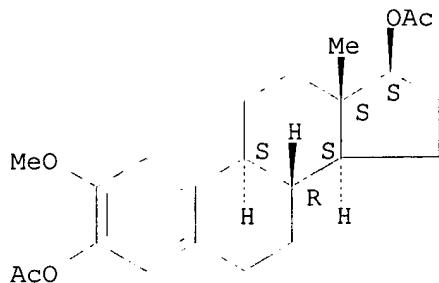
was determined in DMSO/H<sub>2</sub>O (2:1) at room temperature, and the 3,4-quinones were more

stable than the 2,3-quinones. The four quinones directly reacted with calf thymus DNA to form DNA adducts analyzed by the 32P-postlabeling method. The adducts were compared to those formed when the corresponding CE were activated by horseradish peroxidase (HRP) to bind to DNA. The E1- and E2-2,3-quinones formed much higher levels of DNA adducts than the corresponding 3,4-quinones. In addition, many of the adducts (70-90%) formed by the E1- and E2-2,3-quinones appeared to be the same as those formed by activation of 2-OHE1 or 2-OHE2 by HRP to bind to DNA. Little overlap was observed between the adducts formed by E1- and E2-3,4-quinones and HRP-activated 4-OHE1 and 4-OHE2. Thus, semiquinones and/or quinones are ultimate reactive intermediates in the peroxidative activation of catechol estrogens.

- ST catechol estrogen peroxidase quinone; DNA adduct estrogen quinone peroxidase; estradiol quinone peroxidase hydroxyestradiol DNA; estrone quinone peroxidase hydroxyestrone DNA
- IT Estrogens  
 RL: SPN (Synthetic preparation); PREP (Preparation)  
 (quinones, preparation and DNA adduct formation by, peroxidase-activated catechol estrogen in relation to)
- IT Deoxyribonucleic acids  
 RL: BIOL (Biological study)  
 (adducts, with estrogen quinones, catechol estrogen activation by peroxidase in relation to)
- IT Estrogens  
 RL: BIOL (Biological study)  
 (hydroxy, activation of, by peroxidase, quinone formation in, DNA adducts in relation to)
- IT 7291-57-8 144082-85-9  
 RL: BIOL (Biological study)  
 (C3-deacetylation and demethylation of)
- IT 9003-99-0, Peroxidase  
 RL: BIOL (Biological study)  
 (catechol estrogen activation by, quinone formation in, DNA adducts in relation to)
- IT 83649-26-7 144072-46-8  
 RL: RCT (Reactant); RACT (Reactant or reagent)  
 (deacetylation and demethylation of)
- IT 40551-33-5D, Estra-1(10),4-diene-2,3,17-trione, DNA adducts 40551-34-6D,  
 Estra-1,5(10)-diene-3,4,17-trione, DNA adducts 42261-16-5D, DNA adducts  
 144082-88-2D, DNA adducts  
 RL: FORM (Formation, nonpreparative)  
 (formation of, catechol estrogen activation by peroxidase in relation to)
- IT 23463-05-0P 144082-86-0P  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT  
 (Reactant or reagent)  
 (preparation and acid hydrolysis of)
- IT 362-05-0P, 2-Hydroxyestradiol 362-06-1P, 2-Hydroxyestrone 3131-23-5P,  
 4-Hydroxyestrone 5976-61-4P, 4-Hydroxyestradiol  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT  
 (Reactant or reagent)  
 (preparation and oxidation of)
- IT 40551-33-5P, Estra-1(10),4-diene-2,3,17-trione 40551-34-6P,  
 Estra-1,5(10)-diene-3,4,17-trione 42261-16-5P 144082-88-2P  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT  
 (Reactant or reagent)  
 (preparation and reaction of, with DNA)
- IT 144082-87-1P 144082-89-3P  
 RL: SPN (Synthetic preparation); PREP (Preparation)  
 (preparation of)
- IT 7291-57-8

RL: BIOL (Biological study)  
(C3-deacetylation and demethylation of)  
RN 7291-57-8 HCPLUS  
CN Estra-1,3,5(10)-triene-3,17-diol, 2-methoxy-, diacetate, (17 $\beta$ )- (9CI)  
(CA INDEX NAME)

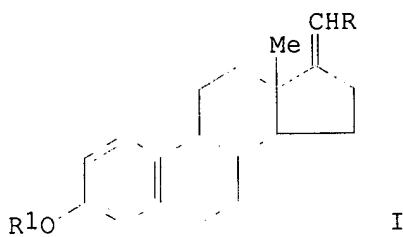
Absolute stereochemistry.



L89 ANSWER 15 OF 22 HCPLUS COPYRIGHT 2003 ACS on STN  
AN 1990:173065 HCPLUS  
DN 112:173065  
ED Entered STN: 12 May 1990  
TI Preparation of 17-methylenestratrienes as contraceptives and drugs for treatment of climacteric disorders  
IN Jungblut, Peter; Wiechert, Rudolf; Bittler, Dieter  
PA Schering A.-G., Fed. Rep. Ger.  
SO Ger. Offen., 4 pp.  
CODEN: GWXXBX  
DT Patent  
LA German  
IC ICM A61K031-57  
ICS A61K031-56; C07J003-00; C07J007-00  
ICA A61K009-06; A61K009-08; A61K009-20; A61K009-50; C12Q001-00  
CC 2-3 (Mammalian Hormones)  
Section cross-reference(s): 32

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	DE 3741801	A1	19890615	DE 1987-3741801	19871207 <--
	EP 320437	A2	19890614	EP 1988-730273	19881205 <--
	EP 320437	A3	19910731		
	R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE				
	CA 1329770	A1	19940524	CA 1988-585132	19881206 <--
	AU 8826653	A1	19890608	AU 1988-26653	19881207 <--
	AU 621844	B2	19920326		
	JP 01197438	A2	19890809	JP 1988-307973	19881207 <--
	US 4977147	A	19901211	US 1988-280803	19881207 <--
PRAI	DE 1987-3741801		19871207 <--		
OS	CASREACT 112:173065; MARPAT 112:173065				
GI					



AB The 17-methylenestratrienes I ( $R = H, Me$ ;  $R1 = H, Me$ , acyl, tetrahydropyranyl) are prepared as contraceptives, drugs for the treatment of hormone-dependent tumors, and drugs for the treatment of climacteric disorders. Compared to estrones, I show less affinity to estrogen receptors and higher cell membrane and lymph vessel permeability. A suspension of  $MePh_3PBr$  in dioxane was treated with a solution of  $BuLi$  in hexane, followed by the addition of 3-(tetrahydropyran-2-yloxy)-1,3,5(10)-estratrien-17-one, to give 17-methylene-3-(tetrahydropyran-2-yloxy)-1,3,5(10)-estratriene. This was treated with  $H_2SO_4$  in  $MeOH$ , to give 17-methylene-1,3,5(10)-estratrien-3-ol (II). Pills contained II 0.050, lactose 46.450, starch 26.800, PVP 3.000 and talc 3.700 mg/each. In uterus growth tests with young rats, II showed 1/70th of the uterotrophic activity of estradiol.

ST methylenestratriene prepn contraceptive anticancer; estratriene methylene contraceptive anticancer

IT Contraceptives

Neoplasm inhibitors  
(methylenestratrienes)

IT Climacteric (animal)

(treatment of, with methylenestratrienes)

IT 1530-32-1 1779-49-3, Methyltriphenylphosphonium bromide

RL: RCT (Reactant); RACT (Reactant or reagent)

(Wittig reaction of, with estratrienone derivative)

IT 57711-40-7

RL: RCT (Reactant); RACT (Reactant or reagent)

(Wittig reaction of, with ethyltriphenylphosphonium bromide)

IT 7103-48-2

RL: RCT (Reactant); RACT (Reactant or reagent)

(Wittig reaction of, with methyltriphenylphosphonium bromide)

IT 126400-73-5P

RL: RCT (Reactant); PREP (Preparation); RACT (Reactant or reagent)

(preparation and hydrolysis of)

IT 4350-65-6P 32043-13-3P 34111-53-0P 35456-72-5P 77257-06-8P

126400-71-3P 126400-72-4P

RL: PREP (Preparation)

(preparation of, as contraceptive and neoplasm inhibitor and drug for treatment of climacteric disorders)

IT 34111-53-0P

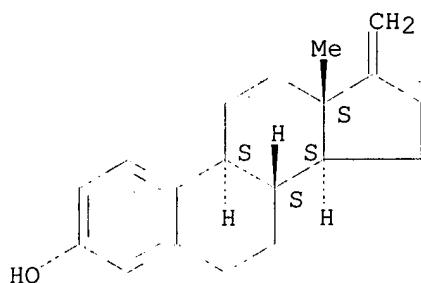
RL: PREP (Preparation)

(preparation of, as contraceptive and neoplasm inhibitor and drug for treatment of climacteric disorders)

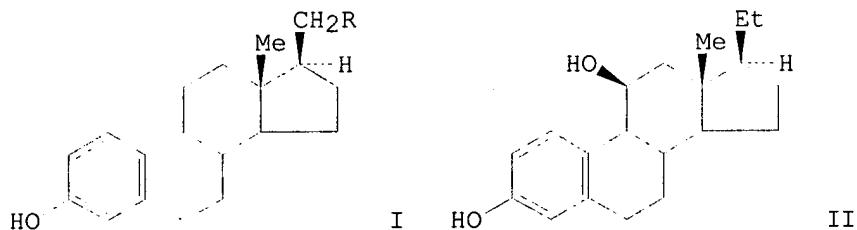
RN 34111-53-0 HCAPLUS

CN Estra-1,3,5(10)-trien-3-ol, 17-methylene- (7CI, 8CI, 9CI) (CA INDEX NAME)

Absolute stereochemistry.



L89 ANSWER 16 OF 22 HCAPLUS COPYRIGHT 2003 ACS on STN  
 AN 1989:423774 HCAPLUS  
 DN 111:23774  
 ED Entered STN: 21 Jul 1989  
 TI 17-Desoxy estrogen analogs  
 AU Peters, Richard H.; Crowe, David F.; Avery, Mitchell A.; Chong, Wesley K.  
 M.; Tanabe, Masato  
 CS Bio-Org. Chem. Lab., SRI Int., Menlo Park, CA, 94025, USA  
 SO Journal of Medicinal Chemistry (1989), 32(7), 1642-52  
 CODEN: JMCMAR; ISSN: 0022-2623  
 DT Journal  
 LA English  
 CC 32-3 (Steroids)  
 Section cross-reference(s): 2  
 OS CASREACT 111:23774  
 GI



AB A series of 17-substituted 17-desoxyestratrienes, e.g. I ( $R = H, Me$ ) and II, were synthesized and tested as potential postcoital antifertility agents. Estrogen-relative binding affinities were determined; in vivo assays for estrogenic and postcoital antifertility activity were conducted in rats, and selected candidate compds. were further tested for estrogenic activity in monkeys. In the rat, I ( $R = H, Me$ ) and II have low estrogenic activity while retaining potent antifertility activity. Structural modifications at the outset included a variety of 17-substituents and an omission of the 17-oxygen functionality, which was previously thought to be necessary for potent activity. The 17 $\beta$ -Et side chain exhibited the greatest antifertility activity with the largest separation ratio to estrogenicity. Nuclear modification of 17-desoxyethylestrane derivs. at positions 7 and 11 further increased the desired separation of activity, with the 11-hydroxy moiety enhancing separation more than other features.  
 ST desoxy estrogen analog prepn antifertility  
 IT Estrogens  
 RL: RCT (Reactant); RACT (Reactant or reagent)  
 (17-substituted deoxyestratrienes as)  
 IT Molecular structure-biological activity relationship  
 (antifertility, 17-substituted deoxyestratrienes)

- IT Molecular structure-biological activity relationship  
(estrogenic, 17-substituted deoxyestratrienes)
- IT Fertility  
(inhibitors, 17-substituted deoxyestratrienes as)
- IT 2344-80-1, (Chloromethyl)trimethylsilane  
RL: RCT (Reactant); RACT (Reactant or reagent)  
(Grignard reaction of, with norpregnatrienone derivative)
- IT 53-16-7, reactions 2487-49-2, 7 $\alpha$ -Hydroxyestrone 6803-21-0,  
11 $\beta$ -Hydroxyestrone 10448-96-1, 7 $\alpha$ -Methylestrone  
RL: RCT (Reactant); RACT (Reactant or reagent)  
(Wittig reaction of)
- IT 1779-49-3, Methyltriphenylphosphonium bromide  
RL: RCT (Reactant); RACT (Reactant or reagent)  
(Wittig reaction of, with dehydroestrone)
- IT 1530-32-1, Ethyltriphenylphosphonium bromide 1779-51-7,  
Butyltriphenylphosphonium bromide 6228-47-3, Propyltriphenylphosphonium  
bromide  
RL: RCT (Reactant); RACT (Reactant or reagent)  
(Wittig reaction of, with estrone)
- IT 2208-12-0, 6-Dehydroestrone  
RL: RCT (Reactant); RACT (Reactant or reagent)  
(Wittig reaction of, with methyltriphenylphosphonium bromide)
- IT 120661-79-2  
RL: RCT (Reactant); RACT (Reactant or reagent)  
(chlorination of, with phosphorus oxytrichloride)
- IT 50-28-2P, Estradiol, preparation  
RL: PREP (Preparation)  
(estrogenic and antifertility activity of)
- IT 57-63-6 3762-05-8 34816-55-2 50866-95-0 59903-16-1  
RL: RCT (Reactant); RACT (Reactant or reagent)  
(estrogenic and antifertility activity of)
- IT 67530-18-1  
RL: RCT (Reactant); RACT (Reactant or reagent)  
(fluorination of, with piperidinylsulfur trifluoride)
- IT 120476-13-3  
RL: RCT (Reactant); RACT (Reactant or reagent)  
(hydrogenation of)
- IT 100-53-8, Benzyl mercaptan  
RL: RCT (Reactant); RACT (Reactant or reagent)  
(ketalization by, of estrone)
- IT 901-93-9  
RL: RCT (Reactant); RACT (Reactant or reagent)  
(ketalization of, with benzyl mercaptan)
- IT 917-54-4, Methylolithium  
RL: RCT (Reactant); RACT (Reactant or reagent)  
(methylation by, of hydroxynorpregnatrienone)
- IT 591-51-5, Phenyllithium  
RL: RCT (Reactant); RACT (Reactant or reagent)  
(phenylation by, of estratetraenone derivative)
- IT 17748-68-4  
RL: RCT (Reactant); RACT (Reactant or reagent)  
(phenylation of, with phenyllithium)
- IT 1787-44-6P  
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT  
(Reactant or reagent)  
(preparation and Wittig reaction of, with estrone)
- IT 120476-12-2P  
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT  
(Reactant or reagent)  
(preparation and deacetylation of)
- IT 120496-23-3P  
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT  
(Reactant or reagent)

(preparation and dehydrochlorination of)

IT 120475-89-0P  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation and dehydroiodination of)

IT 117864-98-9P  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation and deketalization of)

IT 120476-02-0P  
 RL: SPN (Synthetic preparation); PREP (Preparation)

(preparation and desilylation-dehydration of)

IT 3342-64-1P 5982-51-4P 7628-02-6P 16934-51-3P 59077-04-2P,  
 19-Norpregna-1,3,5(10)-trien-3-ol 59452-14-1P 59452-15-2P  
 59452-16-3P, 19,21-Dinorchola-1,3,5(10)-trien-3-ol 60037-62-9P  
 65928-98-5P 73271-91-7P 84510-05-4P 97560-70-8P,  
 19-Norpregna-1,3,5(10),20-tetraen-3-ol 108887-34-9P 120475-91-4P  
 120475-92-5P 120475-94-7P 120475-96-9P 120476-01-9P 120476-03-1P  
 120476-04-2P 120476-05-3P 120476-06-4P 120476-07-5P 120476-09-7P  
 120476-11-1P  
 RL: SPN (Synthetic preparation); PREP (Preparation)

(preparation and estrogenic and antifertility activity of)

IT 33946-34-8P  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation and fluorination by, of acetoxy norpregnatrienone)

IT 120475-95-8P 120476-08-6P 120476-10-0P  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation and hydrogenation of)

IT 120475-88-9P  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation and iodination of)

IT 120475-99-2P  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation and selective de-O-methylation of)

IT 65929-00-2P  
 RL: SPN (Synthetic preparation); PREP (Preparation)

(preparation of)

IT 4736-62-3P 34111-53-0P 99898-92-7P, 19-Norpregna-1,3,5(10)-trien-20-yn-3-ol 102177-29-7P 120475-90-3P 120475-93-6P  
 120475-97-0P 120574-27-8P 120574-28-9P  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation, hydrogenation, and estrogenic and antifertility activity of)

IT 120475-98-1P 120476-00-8P  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation, methylation, and estrogenic and antifertility activity of)

IT 95943-73-0P  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation, reduction, and estrogenic and antifertility activity of)

IT 62437-99-4  
 RL: RCT (Reactant); RACT (Reactant or reagent)

(reaction of, with estrone)

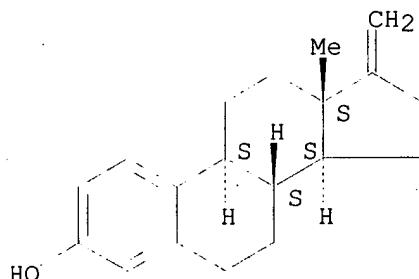
IT 994-30-9, Triethylchlorosilane  
 RL: RCT (Reactant); RACT (Reactant or reagent)

(reaction of, with ethynylestratriene derivative)

IT 7783-60-0, Sulfur tetrafluoride  
 RL: RCT (Reactant); RACT (Reactant or reagent)

(reaction of, with piperidine derivative)  
IT 3768-56-7  
RL: RCT (Reactant); RACT (Reactant or reagent)  
(reaction of, with sulfur tetrafluoride)  
IT 603-35-0, reactions  
RL: RCT (Reactant); RACT (Reactant or reagent)  
(reaction of, with trideuteromethyl bromide)  
IT 1111-88-2  
RL: RCT (Reactant); RACT (Reactant or reagent)  
(reaction of, with triphenylphosphine)  
IT 1667-98-7  
RL: RCT (Reactant); RACT (Reactant or reagent)  
(reaction with hydrazine and estrogenic and antifertility activity of)  
IT 120574-29-0  
RL: RCT (Reactant); RACT (Reactant or reagent)  
(saponification of)  
IT 34111-53-0P  
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT  
(Reactant or reagent)  
(preparation, hydrogenation, and estrogenic and antifertility activity of)  
RN 34111-53-0 HCPLUS  
CN Estra-1,3,5(10)-trien-3-ol, 17-methylene- (7CI, 8CI, 9CI) (CA INDEX NAME)

Absolute stereochemistry.



L89 ANSWER 17 OF 22 HCPLUS COPYRIGHT 2003 ACS on STN  
AN 1981:462492 HCPLUS  
DN 95:62492  
ED Entered STN: 12 May 1984  
TI D-Homo steroids from oxidation of 17-methylene steroids by thallium(III) nitrate  
AU Forcellese, Maria Luigia; Camerini, Elio; Ruffini, Bruna; Mincione, Enrico  
CS Cent. Stud. Chim. Sostanze Org. Nat., CNR, Italy  
SO Journal of Organic Chemistry (1981), 46(16), 3326-8  
CODEN: JOCEAH; ISSN: 0022-3263  
DT Journal  
LA English  
CC 32-4 (Steroids)  
AB Thallium (III)-nitrate reacts with 17-methylene steroids to form D-homo-17 $\alpha$ -methoxy-17 $\alpha$ -oxo compds. via ring enlargement, enolization, oxythallation, and methanolysis.  
ST methylene steroid thallium oxidn; homosteroid methoxyoxo  
IT Rearrangement  
(in thallium nitrate oxidation of methylene steroids, methoxyoxo homosteroids from)  
IT Oxidation  
(of methylene steroids by thallium nitrate, methoxyoxo homosteroids from)  
IT D-Homosteroids  
RL: SPN (Synthetic preparation); PREP (Preparation)

(preparation of, by thallium nitrate oxidation of methylene steroids)  
IT 53-16-7P, preparation  
RL: RCT (Reactant); PREP (Preparation); RACT (Reactant or reagent)  
(methylenation of)

IT 13746-98-0  
RL: RCT (Reactant); RACT (Reactant or reagent)  
(oxidation reagent, for methylene steroids)

IT 34111-53-0P  
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT  
(Reactant or reagent)  
(preparation and acetylation of)

IT 77257-05-7P 77257-07-9P  
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT  
(Reactant or reagent)  
(preparation and hydrolysis of)

IT 77257-04-6P  
RL: SPN (Synthetic preparation); PREP (Preparation)  
(preparation and hydrolysis of)

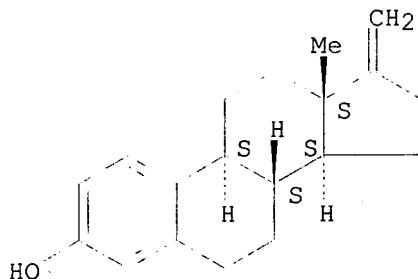
IT 77257-08-0P 77257-09-1P 77257-10-4P  
RL: SPN (Synthetic preparation); PREP (Preparation)  
(preparation of)

IT 853-22-5 1164-94-9 77257-06-8  
RL: RCT (Reactant); RACT (Reactant or reagent)  
(thallium nitrate oxidation of)

IT 34111-53-0P  
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT  
(Reactant or reagent)  
(preparation and acetylation of)

RN 34111-53-0 HCPLUS  
CN Estra-1,3,5(10)-trien-3-ol, 17-methylene- (7CI, 8CI, 9CI) (CA INDEX NAME)

Absolute stereochemistry.



L89 ANSWER 18 OF 22 HCPLUS COPYRIGHT 2003 ACS on STN  
AN 1979:121859 HCPLUS  
DN 90:121859  
ED Entered STN: 12 May 1984  
TI Clinical analysis on steroids. Part V. Synthesis of 2,3,17 $\beta$ -trihydroxyestra-1,3,5(10)-trien-6-one and its related compounds  
AU Nakagawa, Akiko; Ohuchi, Ryoko; Yoshizawa, Itsuo  
CS Hokkaido Inst. Pharm. Sci., Hokkaido, Japan  
SO Chemical & Pharmaceutical Bulletin (1978), 26(11), 3567-71  
CODEN: CPBTAL; ISSN: 0009-2363  
DT Journal  
LA English  
CC 32-3 (Steroids)  
AB Allylic oxidation of 2,3-dimethoxy-17 $\beta$ -acetoxyestra-1,3,5(10)-triene and subsequent saponification gave 17 $\beta$ -hydroxy-2,3-dimethoxyestra-1,3,5(10)-trien-6-one, which was treated with pyridine containing HCl at 200° for 15 min to give 2,3,17 $\beta$ -trihydroxyestra-1,3,5(10)-trien-6-one.

Similarly, 3,17 $\beta$ -diacetoxy-2-methoxyestra-1,3,5(10)-triene gave  
 3,17 $\beta$ -dihydroxy-2-methoxyestra-1,3,5(10)-trien-6-one and  
 2,17 $\beta$ -diacetoxy-3-methoxyestra-1,3,5(10)-triene gave  
 2,17 $\beta$ -dihydroxy-3-methoxyestra-1,3,5(10)-triene-6-one.

ST oxidn allylic methoxyestraiene; estratrienol acetate allylic oxidn;  
 estratrienone trihydroxy; methoxyestraiene

IT Oxidation

(allylic, of unsatd. 19-norsteroids)

IT 19-Norsteroids

RL: RCT (Reactant); RACT (Reactant or reagent)  
 (unsatd., allylic oxidation of)

IT 5976-65-8 5976-67-0

RL: RCT (Reactant); RACT (Reactant or reagent)  
 (acetylation of)

IT 7291-57-8

RL: RCT (Reactant); RACT (Reactant or reagent)  
 (allylic oxidation of)

IT 69540-61-0P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT  
 (Reactant or reagent)  
 (preparation and acetylation of)

IT 5976-70-5P 7002-81-5P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT  
 (Reactant or reagent)  
 (preparation and allylic oxidation of)

IT 69540-59-6P 69540-62-1P 69591-42-0P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT  
 (Reactant or reagent)  
 (preparation and deacetylation of)

IT 69540-60-9P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT  
 (Reactant or reagent)  
 (preparation and demethylation of)

IT 68129-02-2P 69540-63-2P 69540-64-3P

RL: SPN (Synthetic preparation); PREP (Preparation)  
 (preparation of)

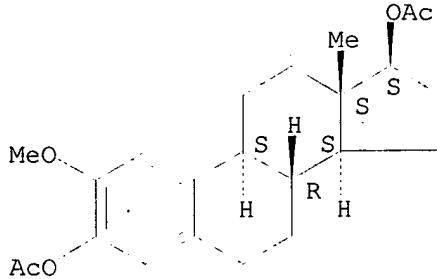
IT 7291-57-8

RL: RCT (Reactant); RACT (Reactant or reagent)  
 (allylic oxidation of)

RN 7291-57-8 HCPLUS

CN Estra-1,3,5(10)-triene-3,17-diol, 2-methoxy-, diacetate, (17 $\beta$ )- (9CI)  
 (CA INDEX NAME)

Absolute stereochemistry.



L89 ANSWER 19 OF 22 HCPLUS COPYRIGHT 2003 ACS on STN

AN 1976:421725 HCPLUS

DN 85:21725

ED Entered STN: 12 May 1984

TI 19-Norpregna-1,3,5(10)-trien-3-ol and lower alkyl homologs having

IN postcoital antifertility activity  
 PA Crowe, David F.; Peters, Richard H.; Tanabe, Masato; Detre, George

PA Stanford Research Institute, USA

SO U.S., 5 pp.

CODEN: USXXAM

DT Patent

LA English

IC C07J

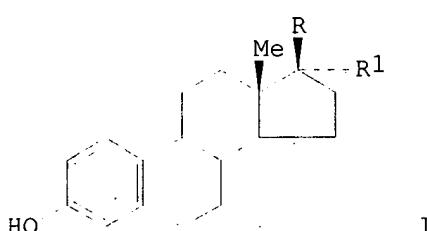
NCL 260397500

CC 32-5 (Steroids)

FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI US 3946052	A	19760323	US 1975-587256	19750616 <--
PRAI US 1975-587256		19750616		<--

GI



AB Estratrienols I (R = Me, Et, Pr, Bu; R1 = H) were prepared by Wittig reaction of I (RR1 = O) with RP+Ph3 Br- followed by hydrogenation over Pd/C. Thus, a solution of 9.5 g estrone in Me2SO was added to a suspension of EtP+Ph3 Br- and NaH in Me2SO. Heating the mixture for 18 hr at 60° yielded 6.8 g I (RR1 = CHMe). Hydrogenation of 500 mg I (RR1 = CHMe) over Pd/C gave 400 mg I (R = Et, R1 = H), which had a 100 fold separation of postcoital antifertility from estrogenic activity as compared with ethynodiol diacetate at 200µg/hk/day orally in rats.

ST norpregnatrienol contraceptive; Wittig estrone; norpregnatriene hydrogenation

IT 19-Norsteroids

RL: RCT (Reactant); RACT (Reactant or reagent)  
 (17β-alkyl-3-hydroxy-1,3,5(10)-unsatd.)

IT Contraceptives

(postcoital, 19-norpregna-1,3,5(10)-trien-3-ol as)

IT 53-16-7

RL: RCT (Reactant); RACT (Reactant or reagent)  
 (Wittig reaction of)

IT 4350-65-6P 34111-53-0P 59452-12-9P 59452-13-0P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
 (preparation and hydrogenation of)

IT 59077-04-2P

RL: SPN (Synthetic preparation); PREP (Preparation)  
 (preparation and postcoital antifertility activity of)

IT 59452-14-1P 59452-15-2P 59452-16-3P

RL: SPN (Synthetic preparation); PREP (Preparation)  
 (preparation of)

IT 1530-32-1 1779-49-3 1779-51-7 6228-47-3

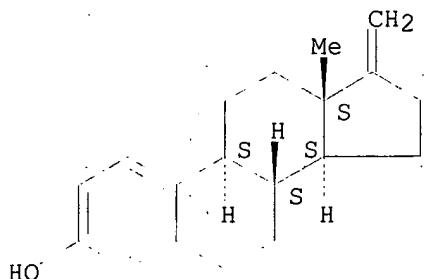
RL: RCT (Reactant); RACT (Reactant or reagent)  
 (reaction of, with estrone)

IT 34111-53-0P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation and hydrogenation of)  
RN 34111-53-0 HCAPLUS  
CN Estra-1,3,5(10)-trien-3-ol, 17-methylene- (7CI, 8CI, 9CI) (CA INDEX NAME)

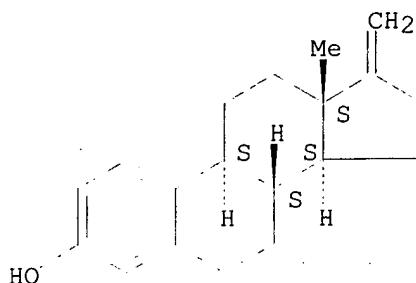
Absolute stereochemistry.



L89 ANSWER 20 OF 22 HCAPLUS COPYRIGHT 2003 ACS on STN  
AN 1971:551978 HCAPLUS  
DN 75:151978  
ED Entered STN: 12 May 1984  
TI 17-Methylenestrane derivatives  
IN Ota, Motokichi; Takegoshi, Toshio; Obata, Kazunaga; Oshima, Yasuo;  
Kasahara, Akira  
PA Daiichi Seiyaku Co., Ltd.  
SO Jpn. Tokkyo Koho, 4 pp.  
CODEN: JAXXAD  
DT Patent  
LA Japanese  
IC C07C; C07D; A61K  
CC 32 (Steroids)  
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	JP 46034421	B4	19711008	JP	19681208 <--
AB	17-Oxoestrane derivative was treated with (Ph <sub>3</sub> PM <sub>e</sub> )X (X=halogen) in the presence of an acidic condensation agent to give the corresponding 17-methylenestrane derivative. Thus, estrone and (Ph <sub>3</sub> PM <sub>e</sub> )Br in Me <sub>2</sub> SO was stirred with tert-BuOK in a N stream to give 17-methylenestra-1,3,5(10)-trien-3-ol. Similarly prepared were 3 more 3-substituted 17-methylenestra-1,3,5(10)-trienes. The products are anticholesterol agents.				
ST	estrane methylene derivs; anticholesterol estranes				
IT	34111-53-0P	RL: SPN (Synthetic preparation); PREP (Preparation) (preparation of)			
IT	34111-53-0P	RL: SPN (Synthetic preparation); PREP (Preparation) (preparation of)			
RN	34111-53-0 HCAPLUS				
CN	Estra-1,3,5(10)-trien-3-ol, 17-methylene- (7CI, 8CI, 9CI) (CA INDEX NAME)				

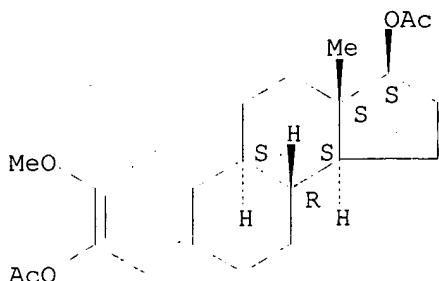
Absolute stereochemistry.



L89 ANSWER 21 OF 22 HCAPLUS COPYRIGHT 2003 ACS on STN  
 AN 1970:516788 HCAPLUS  
 DN 73:116788  
 ED Entered STN: 12 May 1984  
 TI Analytical chemical studies on steroids. XXXVII. Gas chromatography of 2,3-oxygenated estratrienes  
 AU Nambara, Toshio; Iwata, Takehiko; Honma, Seijiro  
 CS Pharm. Inst., Tohoku Univ., Sendai, Japan  
 SO Journal of Chromatography (1970), 50(3), 400-4  
 CODEN: JOCRAM; ISSN: 0021-9673  
 DT Journal  
 LA English  
 CC 4 (Hormones and Related Substances)  
 AB The steroid number (SN) values (W. Van de Heuvel and E. C. Horning, 1962) for estratrienes having O functional group substituents at the 2- and 3-positions were determined by gas chromatog. on a 3% SE-3/Chromosorb W column, with a H flame ionization detector and N carrier gas. The SN contributions of various O functional groups at the 2- and 3-positions were estimated by using estra-1,3,5(10)-triene as a reference compound. The contribution of 2 functional groups on ring A and D was in agreement with the summation of the values characteristic of each substituent. The additivity rule was applicable to the 2,3-oxygenated estratrienes, when the SN contributions of the vicinal functional groups on ring A are considered as a set. The method may be used to identify metabolites derived from modified steroids as well as the naturally occurring estrogens.  
 ST steroids gas chromatog; estratrienes gas chromatog; gas chromatog estratrienes  
 IT Steroids, properties  
 RL: PROC (Process)  
 (chromatog. of)  
 IT Molecular structure-property relationships  
 (chromatographic, of estratriene derivs.)  
 IT 50-28-2, analysis 53-16-7, analysis 53-45-2 53-63-4 362-07-2  
 362-08-3 901-93-9 1035-77-4 1217-09-0 1549-15-1 1743-60-8  
 1839-54-9 2259-89-4 2354-44-1 2529-64-8 2755-14-8 3434-88-6  
 4967-94-6 5150-62-9 5976-55-6 5976-59-0 5976-63-6 5976-65-8  
 7002-81-5 **7291-57-8** 10584-10-8 10584-11-9 14550-57-3  
 16274-22-9 17519-71-0 17553-16-1 18880-67-6 26356-97-8  
 26356-99-0 29741-91-1 29741-92-2 29741-94-4 29755-23-5  
 29755-24-6 29755-25-7 29755-26-8 29755-30-4 29755-31-5  
 29755-32-6 29755-33-7 29755-34-8 29755-43-9 29825-35-2  
 29825-36-3 29825-37-4 29825-39-6 29825-40-9 29825-41-0  
 29825-42-1 29825-43-2 29825-44-3 29825-46-5 29825-47-6  
 29825-48-7 29971-45-7 29971-46-8 29978-30-1  
 RL: PROC (Process)  
 (chromatog. of)  
 IT **7291-57-8**  
 RL: PROC (Process)

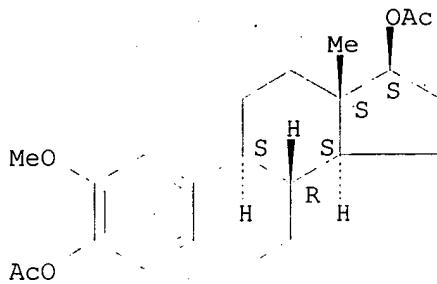
(chromatog. of)  
RN 7291-57-8 HCPLUS  
CN Estra-1,3,5(10)-triene-3,17-diol, 2-methoxy-, diacetate, (17 $\beta$ )- (9CI)  
(CA INDEX NAME)

Absolute stereochemistry.



L89 ANSWER 22 OF 22 HCPLUS COPYRIGHT 2003 ACS on STN  
AN 1970:121765 HCPLUS  
DN 72:121765  
ED Entered STN: 12 May 1984  
TI Analytical chemical studies on steroids. XXXIV. Steroid conjugates.  
III. New syntheses of 2-methoxyestrogens  
AU Nambara, Toshio; Honma, Seijiro; Akiyama, Setsuko  
CS Pharm. Inst., Tohoku Univ., Sendai, Japan  
SO Chemical & Pharmaceutical Bulletin (1970), 18(3), 474-80  
CODEN: CPBTAL; ISSN: 0009-2363  
DT Journal  
LA English  
CC 32 (Steroids)  
OS CASREACT 72:121765  
AB New synthetic routes leading to the 2-methoxyestrogens from the readily available compds. were investigated. Utilization of both Friedel-Crafts and Baeyer-Villiger reactions with estrone and estradiol 3-methyl ethers gave the desired 2-methoxyestrogens in overall yield of .apprx.50%. Fries rearrangement with estrone acetate and Friedel-Crafts reaction with 2-methoxy-3-deoxyestrogens were also undertaken. The chemical shifts of the aromatic protons of the 2,3-substituted estratrienes are collected in tables.  
ST estrogens methoxy; methoxy estrogens; estrenols methoxy  
IT 19-Norsteroids  
RL: RCT (Reactant); RACT (Reactant or reagent)  
(2-methoxy)  
IT 362-07-2P 362-08-3P 2259-89-4P 7291-57-8P 17519-71-0P  
17553-16-1P 26356-51-4P 26356-52-5P 26356-53-6P 26356-54-7P  
26356-93-4P 26356-96-7P 26356-97-8P 26356-99-0P 26357-00-6P  
26357-02-8P 26357-03-9P 26357-04-0P 26357-05-1P 26357-06-2P  
26357-07-3P 26362-43-6P 26362-44-7P 26517-50-0P  
RL: SPN (Synthetic preparation); PREP (Preparation)  
(preparation of)  
IT 7291-57-8P  
RL: SPN (Synthetic preparation); PREP (Preparation)  
(preparation of)  
RN 7291-57-8 HCPLUS  
CN Estra-1,3,5(10)-triene-3,17-diol, 2-methoxy-, diacetate, (17 $\beta$ )- (9CI)  
(CA INDEX NAME)

Absolute stereochemistry.



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L80 ANSWER 1 OF 3 HCAPLUS COPYRIGHT 2003 ACS on STN  
 AN 2003:719252 HCAPLUS  
 DN 139:224972  
 ED Entered STN: 14 Sep 2003  
 TI Synthesis of 2-methoxyestradiol derivatives and uses as antiangiogenic agents  
 IN Lavallee, Theresa M.; Pribluda, Victor S.; Simons, Jonathan; Mabjeesh, Nicola; Giannakakou, Paraskevi  
 PA Entremed, Inc., USA  
 SO PCT Int. Appl., 77 pp.  
 CODEN: PIXXD2  
 DT Patent  
 LA English  
 IC ICM: A61K  
 CC 2-4 (Mammalian Hormones)  
 Section cross-reference(s): 32

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2003073985	A2	20030912	WO 2003-US5898	20030227 <--
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG	

PRAI US 2002-361267P P 20020301 <--

AB Compns. and methods for treating mammalian disease characterized by undesirable angiogenesis and for controlling a number of angiogenesis-related events, conditions, or substances, by administering derivs. of 2-methoxyestradiol of general formula (I) wherein the variables are defined in the specification.

ST estrogen methoxyestradiol analogs angiogenesis inhibitor VEGF DR5 HIFalpha  
 IT Apoptosis

(2-ME2-induced; synthesis of 2-methoxyestradiol derivs. and uses as antiangiogenic agents)

IT Cytokine receptors

RL: BSU (Biological study, unclassified); BIOL (Biological study) (DR5 (death receptor 5); synthesis of 2-methoxyestradiol derivs. and uses as antiangiogenic agents)

IT Transcription factors

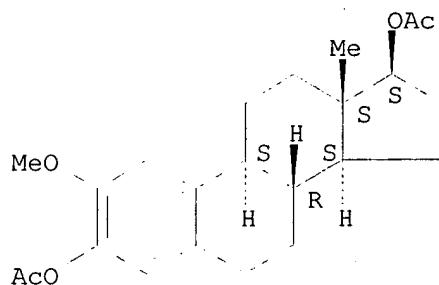
- RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(HIF-1 $\alpha$  (hypoxia-inducible factor 1 $\alpha$ ); synthesis of  
2-methoxyestradiol derivs. and uses as antiangiogenic agents)
- IT Blood vessel  
(endothelium; synthesis of 2-methoxyestradiol derivs. and uses as  
antiangiogenic agents)
- IT Transcriptional regulation  
(of HIF-1 $\alpha$ , 2-ME2-inhibited; synthesis of 2-methoxyestradiol  
derivs. and uses as antiangiogenic agents)
- IT Angiogenesis  
Angiogenesis inhibitors  
Human  
(synthesis of 2-methoxyestradiol derivs. and uses as antiangiogenic  
agents)
- IT Estrogens  
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); BIOL  
(Biological study); PREP (Preparation)  
(synthesis of 2-methoxyestradiol derivs. and uses as antiangiogenic  
agents)
- IT 127464-60-2, Vascular Endothelial Growth Factor  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(synthesis of 2-methoxyestradiol derivs. and uses as antiangiogenic  
agents)
- IT 362-07-2DP, 2-Methoxyestradiol, derivs. and analogs 362-07-2P,  
2-Methoxyestradiol  
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic  
preparation); BIOL (Biological study); PREP (Preparation); RACT (Reactant  
or reagent)  
(synthesis of 2-methoxyestradiol derivs. and uses as antiangiogenic  
agents)
- IT 50-00-0, Formaldehyde, reactions 50-28-2D, Estradiol, derivs. and  
analogs 53-16-7, Estrone, reactions 64-18-6, Formic acid, reactions  
64-19-7, Acetic acid, reactions 67-68-5, Methyl sulfoxide, reactions  
68-12-2, DMF, reactions 71-36-3, 1-Butanol, reactions 75-09-2,  
Methylene chloride, reactions 79-37-8, Oxalyl chloride 100-39-0,  
Benzyl bromide 106-95-6, Allyl bromide, reactions 109-99-9, THF,  
reactions 111-46-6, Diethylene glycol, reactions 121-44-8,  
Triethylamine, reactions 141-78-6, Ethyl acetate, reactions 302-01-2,  
Hydrazine, reactions 362-08-3, 2-Methoxyestrone 362-08-3D,  
2-Methoxyestrone, olefin analogs 584-08-7, Potassium carbonate  
1157-87-5, AH3 1530-32-1, Ethyl triphenylphosphonium bromide  
1779-49-3, Methyltriphenylphosphonium bromide 1779-51-7, Butyl  
triphenylphosphonium bromide 4111-54-0, Lithium diisopropyl amide  
4784-77-4, Crotyl bromide 5815-08-7, tert-Butoxy  
bis(dimethylamino)methane 6228-47-3, Propyl triphenylphosphonium bromide  
7447-41-8, Lithium chloride, reactions 7632-00-0, Sodium nitrite  
7693-26-7, Potassium hydride 16853-85-3, Lithium aluminum hydride  
17455-13-9, 18-Crown-6 17640-15-2, Methyl cyanoformate 41233-93-6,  
Potassium-tert-amylate 431901-79-0 431901-81-4 431901-84-7  
431901-85-8 431901-89-2  
RL: RCT (Reactant); RACT (Reactant or reagent)  
(synthesis of 2-methoxyestradiol derivs. and uses as antiangiogenic  
agents)
- IT 53-63-4P, Estra-1,3,5(10)-trien-3-ol  
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT  
(Reactant or reagent)  
(synthesis of 2-methoxyestradiol derivs. and uses as antiangiogenic  
agents)
- IT 362-07-2DP, 2-Methoxyestradiol, alkyl analogs 4953-96-2P 6298-51-7P  
6301-87-7P 6599-97-9P 7291-57-8P 10332-20-4P 26356-54-7DP,  
alkyl derivs 26356-54-7DP, alkyl derivs. 26356-54-7P 26357-07-3DP,  
16 $\alpha$ -alkyl derivs. 26357-07-3P 32162-96-2P 34111-53-0P  
93949-26-9P 165619-07-8P 229486-18-4P 431901-68-7P

431901-69-8P 431901-70-1P 431901-71-2P 431901-72-3P  
 431901-77-8P 431901-78-9P 431901-80-3DP, alkyl derivs.  
 431901-89-2DP, alkyl analogs 431901-90-5P 431901-91-6P 431901-92-7P  
 431901-93-8P 431901-98-3P 431901-99-4P 431902-01-1P 431902-02-2P  
 431902-03-3P 431902-04-4P 431902-05-5P 431902-06-6P 431902-09-9P  
 438044-30-5P 464924-32-1P 594873-85-5P 594873-86-6P 594873-87-7P  
 RL: SPN (Synthetic preparation); PREP (Preparation)  
 (synthesis of 2-methoxyestradiol derivs. and uses as antiangiogenic agents)

IT 7291-57-8P 34111-53-0P 229486-18-4P  
 431901-68-7P 431901-70-1P 431901-71-2P  
 431901-77-8P 431901-78-9P  
 RL: SPN (Synthetic preparation); PREP (Preparation)  
 (synthesis of 2-methoxyestradiol derivs. and uses as antiangiogenic agents)

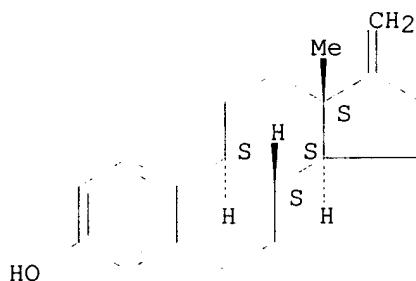
RN 7291-57-8 HCPLUS  
 CN Estra-1,3,5(10)-triene-3,17-diol, 2-methoxy-, diacetate, (17 $\beta$ )- (9CI)  
 (CA INDEX NAME)

Absolute stereochemistry.



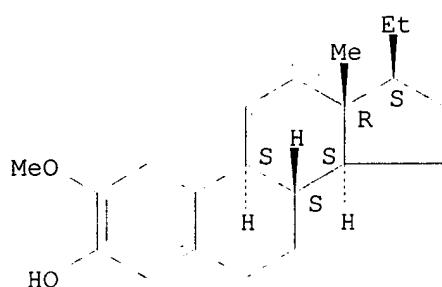
RN 34111-53-0 HCPLUS  
 CN Estra-1,3,5(10)-triene-3-ol, 17-methylene- (7CI, 8CI, 9CI) (CA INDEX NAME)

Absolute stereochemistry.



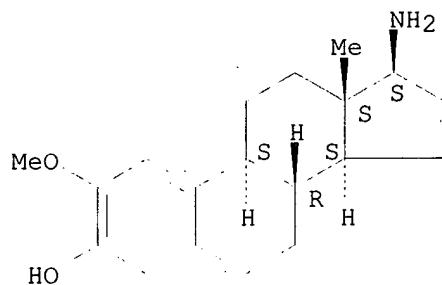
RN 229486-18-4 HCPLUS  
 CN 19-Norpregna-1,3,5(10)-trien-3-ol, 2-methoxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



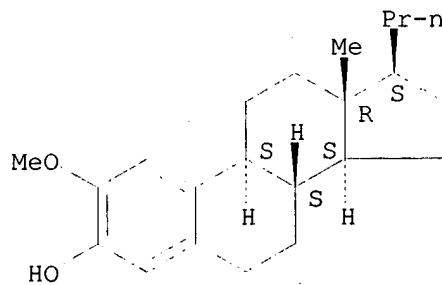
RN 431901-68-7 HCAPLUS  
 CN Estra-1,3,5(10)-trien-3-ol, 17-amino-2-methoxy-, (17 $\beta$ )- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



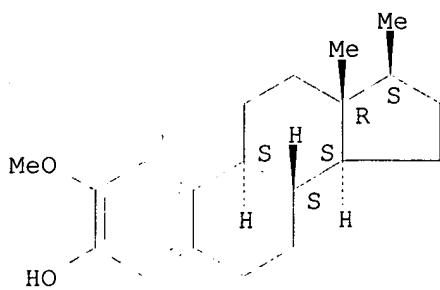
RN 431901-70-1 HCAPLUS  
 CN Estra-1,3,5(10)-trien-3-ol, 2-methoxy-17-propyl-, (17 $\beta$ )- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

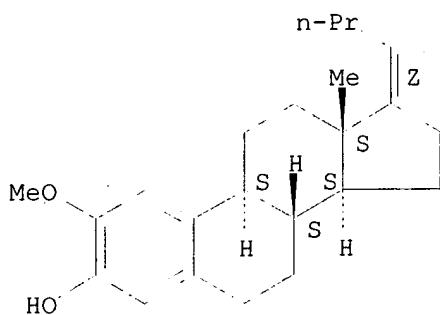


RN 431901-71-2 HCAPLUS  
 CN Estra-1,3,5(10)-trien-3-ol, 2-methoxy-17-methyl-, (17 $\beta$ )- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



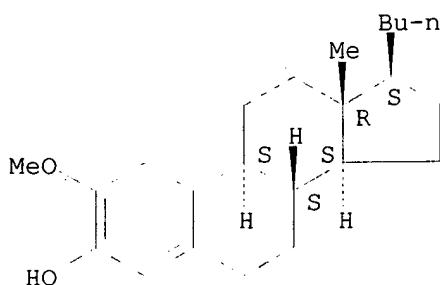
RN 431901-77-8 HCAPLUS

CN 19,21-Dinorchola-1,3(10),17(20)-tetraen-3-ol, 2-methoxy-, (17Z)- (9CI)  
(CA INDEX NAME)Absolute stereochemistry.  
Double bond geometry as shown.

RN 431901-78-9 HCAPLUS

CN 19,21-Dinorchola-1,3(10)-trien-3-ol, 2-methoxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L80 ANSWER 2 OF 3 HCAPLUS COPYRIGHT 2003 ACS on STN

AN 2002:488275 HCAPLUS

DN 137:47357

ED Entered STN: 28 Jun 2002

TI Preparation of 2-methoxyestradiol derivatives as antiangiogenic agents

IN Agoston, Gregory E.; Shah, Jamshed H.; Hunsucker,  
Kimberly A.; Pribluda, Victor S.; Lavallee, Theresa  
M.; Green, Shawn J.; Herbstritt, Christopher J.;  
Zhan, Xiaoguo H.; Treston, Anthony M.

PA USA

SO U.S. Pat. Appl. Publ., 37 pp., Cont.-in-part of U. S. Ser. No. 933,894.  
CODEN: USXXCO

DT Patent  
 LA English  
 IC ICM C07J041-00  
 ICS C07J043-00; C07J001-00; A61K031-704; A61K031-58; A61K031-56;  
 C07C247-00; A61K031-655; C07J009-00

NCL 552544000

CC 32-3 (Steroids)

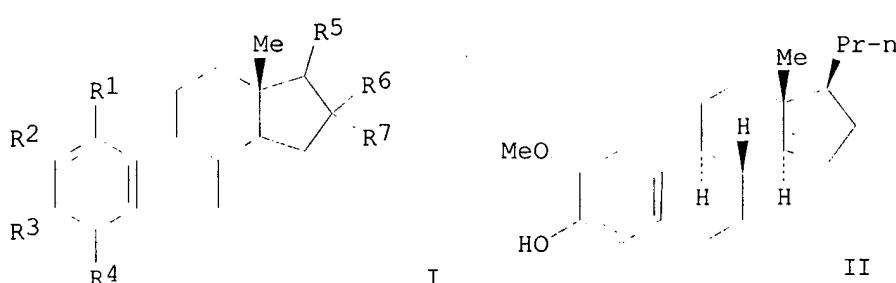
Section cross-reference(s): 1

FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2002082433	A1	20020627	US 2001-939208	20010824 <--
PRAI	US 2000-641327	A2	20000818	<--	
	US 2000-253385P	P	20001127	<--	
	US 2000-255302P	P	20001213	<--	
	US 2001-278250P	P	20010323	<--	
	US 2001-933894	A2	20010821	<--	

OS MARPAT 137:47357

GI



AB 2-Methoxyestradiol derivs. of formula I [R1, R4 = H, halo, CN, alkyl, OH, NH<sub>2</sub>, etc.; R2 = N<sub>3</sub>, CN, OMe, alkenyl, alkynyl, alkoxy, NH<sub>2</sub>, etc.; R3 = OH, OAc; R5 = alkyl, alkenyl, (di)alkylamino, OH, alkylene, etc.; R6, R7 = H, alkyl, alkenyl, alkynyl, halo, etc.] are prepared for treating mammalian disease characterized by undesirable angiogenesis. Thus, II was prepared from 2-methoxyestradiol and propyltriphenylphosphonium bromide. The IC<sub>50</sub> of II against MDA-MB-231 breast tumor cells was 51.31 μM.

ST methoxyestradiol deriv prepn antiangiogenic; estradiol deriv prepn antiangiogenic; antitumor methoxyestradiol deriv prepn; antimitotic methoxyestradiol deriv prepn

IT Structure-activity relationship  
 (antitumor; preparation of 2-methoxyestradiol derivs. as antiangiogenic agents)

IT Mitosis  
 (inhibitors; preparation of 2-methoxyestradiol derivs. as antiangiogenic agents)

IT Angiogenesis inhibitors

Antitumor agents

Human

Mammary gland, neoplasm

Neoplasm

(preparation of 2-methoxyestradiol derivs. as antiangiogenic agents)

IT 362-07-2, 2-Methoxyestradiol

RL: PAC (Pharmacological activity); RCT (Reactant); BIOL (Biological study); RACT (Reactant or reagent)

(preparation of 2-methoxyestradiol derivs. as antiangiogenic agents)

IT 53-63-4P, Estra-1,3,5(10)-trien-3-ol 6301-87-7P 431901-72-3P

431901-73-4P 431901-75-6P 431901-77-8P 431901-91-6P

RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic

preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses) (preparation of 2-methoxyestradiol derivs. as antiangiogenic agents)

IT 1818-12-8P 4953-96-2P 6298-51-7P 6599-97-9P 7291-57-8P  
 10332-20-4P 32162-96-2P 41259-43-2P 94440-60-5P 165619-07-8P  
 165881-61-8P 229486-18-4P 431901-68-7P 431901-69-8P  
**431901-70-1P 431901-71-2P 431901-74-5P**  
**431901-78-9P 431901-87-0P 431901-90-5P 431901-92-7P**  
**431901-93-8P 431901-94-9P 431901-95-0P 431901-96-1P**  
**431901-97-2P 431901-98-3P 431901-99-4P 431902-00-0P**  
**431902-01-1P 431902-02-2P 431902-03-3P 431902-04-4P 431902-05-5P**  
**431902-06-6P 431902-07-7P 431902-08-8P 431902-09-9P**  
**438044-29-2P 438044-30-5P 438044-35-0P**

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

IT (preparation of 2-methoxyestradiol derivs. as antiangiogenic agents)  
 53-16-7, Estrone, reactions 106-95-6, Allyl bromide, reactions  
 1779-51-7, Butyltriphenylphosphonium bromide 4784-77-4, Crotyl bromide  
 5815-08-7 6228-47-3, Propyltriphenylphosphonium bromide

RL: RCT (Reactant); RACT (Reactant or reagent)

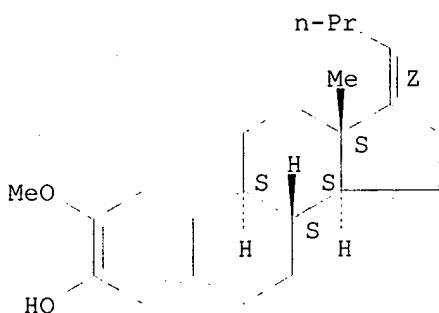
IT (preparation of 2-methoxyestradiol derivs. as antiangiogenic agents)  
 26356-54-7P 26357-07-3P 93949-26-9P 431901-79-0P 431901-81-4P  
 431901-82-5P 431901-83-6P 431901-84-7P 431901-85-8P 431901-89-2P  
 438044-31-6P 438044-32-7P 438044-33-8P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

IT (preparation of 2-methoxyestradiol derivs. as antiangiogenic agents)  
**431901-77-8P**  
 RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

RN 431901-77-8 HCPLUS  
 CN 19,21-Dinorchola-1,3,5(10),17(20)-tetraen-3-ol, 2-methoxy-, (17Z)- (9CI)  
 (CA INDEX NAME)

Absolute stereochemistry.  
 Double bond geometry as shown.

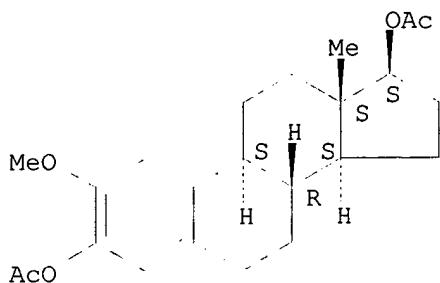


IT 7291-57-8P 229486-18-4P 431901-68-7P  
 431901-70-1P 431901-71-2P 431901-74-5P  
 431901-78-9P 431901-97-2P 438044-29-2P  
 RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of 2-methoxyestradiol derivs. as antiangiogenic agents)

RN 7291-57-8 HCPLUS  
 CN Estra-1,3,5(10)-triene-3,17-diol, 2-methoxy-, diacetate, (17β)- (9CI)  
 (CA INDEX NAME)

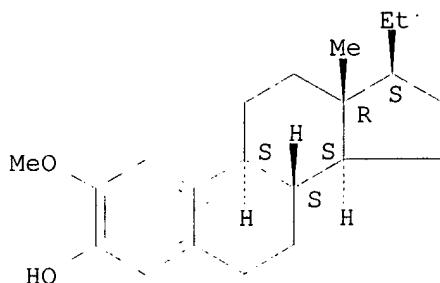
Absolute stereochemistry.



RN 229486-18-4 HCAPLUS

CN 19-Norpregna-1,3,5(10)-trien-3-ol, 2-methoxy- (9CI) (CA INDEX NAME)

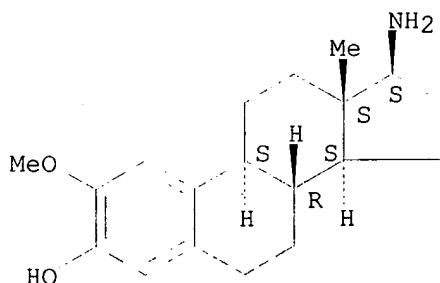
Absolute stereochemistry.



RN 431901-68-7 HCAPLUS

CN Estra-1,3,5(10)-trien-3-ol, 17-amino-2-methoxy-, (17 $\beta$ )- (9CI) (CA INDEX NAME)

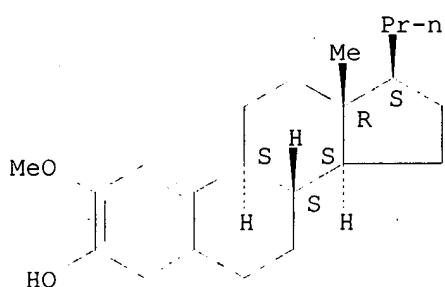
Absolute stereochemistry.



RN 431901-70-1 HCAPLUS

CN Estra-1,3,5(10)-trien-3-ol, 2-methoxy-17-propyl-, (17 $\beta$ )- (9CI) (CA INDEX NAME)

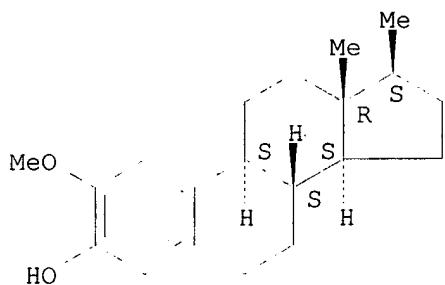
Absolute stereochemistry.



RN 431901-71-2 HCAPLUS

CN Estra-1,3,5(10)-trien-3-ol, 2-methoxy-17-methyl-, (17 $\beta$ )- (9CI) (CA INDEX NAME)

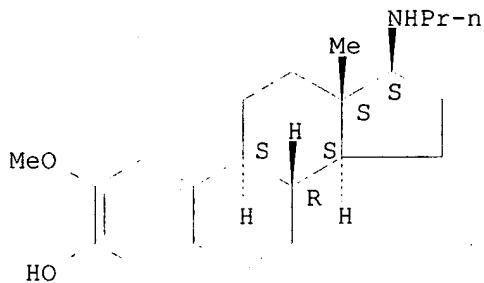
Absolute stereochemistry.



RN 431901-74-5 HCAPLUS

CN Estra-1,3,5(10)-trien-3-ol, 2-methoxy-17-(propylamino)-, (17 $\beta$ )- (9CI) (CA INDEX NAME)

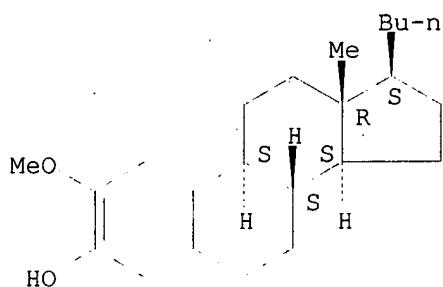
Absolute stereochemistry.



RN 431901-78-9 HCAPLUS

CN 19,21-Dinorchola-1,3,5(10)-trien-3-ol, 2-methoxy- (9CI) (CA INDEX NAME)

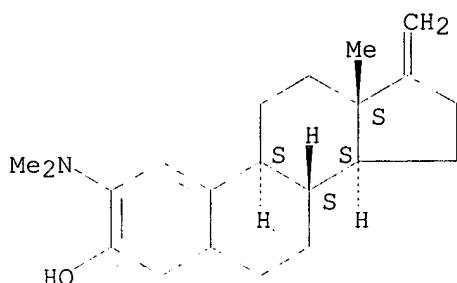
Absolute stereochemistry.



RN 431901-97-2 HCAPLUS

CN Estra-1,3,5(10)-trien-3-ol, 2-(dimethylamino)-17-methylene-, hydrochloride  
(9CI) (CA INDEX NAME)

Absolute stereochemistry.



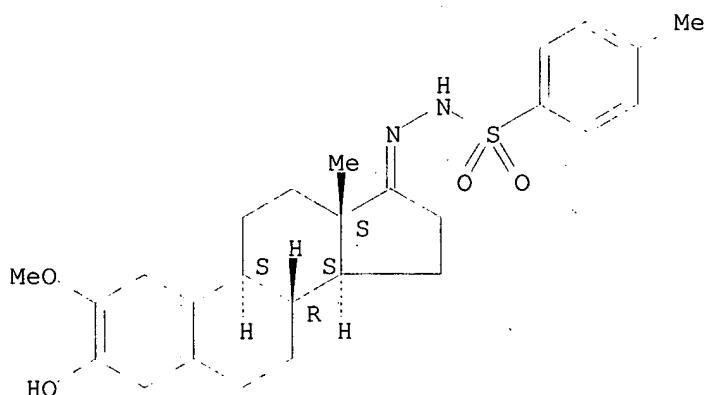
● HCl

RN 438044-29-2 HCAPLUS

CN Benzenesulfonic acid, 4-methyl-, (3-hydroxy-2-methoxyestra-1,3,5(10)-trien-17-ylidene)hydrazide (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry unknown.



L80 ANSWER 3 OF 3 HCAPLUS COPYRIGHT 2003 ACS on STN

AN 2002:408687 HCAPLUS

DN 137:6309

ED Entered STN: 31 May 2002

TI Preparation of 2-methoxyestradiol analogs as antiangiogenic agents  
IN Agoston, Gregory; Shah, Jamshed H.; Hunsucker,  
Kimberly A.; Pribluda, Victor; Lavallee, Theresa M.  
; Green, Shawn J.; Herbstritt, Christopher J.;  
Zhan, Xiaoguo H.; Treston, Anthony

PA Entremed, Inc., USA  
SO PCT Int. Appl., 86 pp.

CODEN: PIXXD2

DT Patent

## LA English

IC ICM CO

## CC 32-3 (Steroids)

## Section cross-references

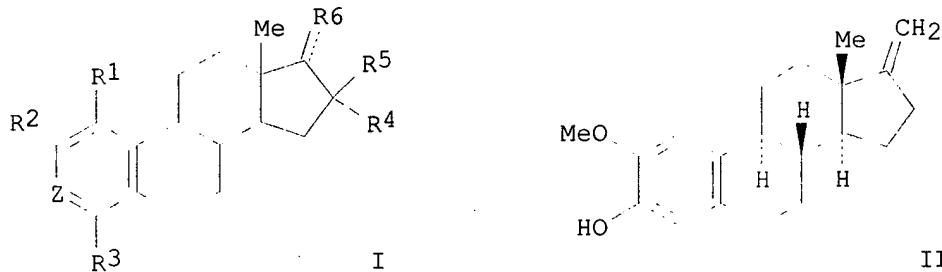
FAN CNT 2

FATE

PI	WO 2002042319	A2	20020530	WO 2001-US26490	20010824 <--
	WO 2002042319	A3	20030313		
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	RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
	AU 2001088386	A5	20020603	AU 2001-88386	20010824 <--
	EP 1343803	A2	20030917	EP 2001-968112	20010824 <--
	R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR			
PRAI	US 2000-253385P	P	20001127	<--	
	US 2000-255302P	P	20001213	<--	
	US 2001-278250P	P	20010323	<--	
	US 2001-933894	A	20010821	<--	
	WO 2001-US26490	W	20010824	<--	

OS MARPAT 137:6309

GI



AB 2-Methoxyestradiol analogs, such as I [R1, R3 = H, halo, CN, alkyl, OH, CH<sub>2</sub>OH, NH<sub>2</sub>, alkylamino; R2 = N<sub>3</sub>, CN, C.tplbond.CR, C=CHR, C.tplbond.CH, OR, amino; R = H, alkyl; Z = COH, COAc; dashed bond = single bond or double bond; R<sub>6</sub> = H, OH, O, oxime, amino, alkyl, alkenyl; R<sub>4</sub>, R<sub>5</sub> = H, alkyl, alkenyl, alkynyl], were prepared for treating mammalian disease characterized by undesirable angiogenesis. Thus, 2-methoxyestradiol analog II was prepared by the reaction of methyltriphenylphosphonium bromide and 2-methoxyestrone. In vitro evaluation against MDA-MB-231 breast tumor cells and HUVEC endothelial cells, II showed IC<sub>50</sub> 0.24±0 and 0.19±0.19 resp.

ST methoxyestradiol deriv prepn antiangiogenic antitumor; estradiol methoxy deriv prepn antiangiogenic antitumor

IT Cell proliferation  
 (inhibition; preparation of 2-methoxyestradiol derivs. as antiangiogenic agents)

IT Mammary gland, neoplasm  
 (inhibitors; preparation of 2-methoxyestradiol derivs. as antiangiogenic agents)

IT Antitumor agents  
 (mammary gland; preparation of 2-methoxyestradiol derivs. as antiangiogenic agents)

IT Angiogenesis inhibitors  
 Human  
 (preparation of 2-methoxyestradiol derivs. as antiangiogenic agents)

IT Estrogens  
 RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)  
 (preparation of 2-methoxyestradiol derivs. as antiangiogenic agents)

IT 53-63-4P, Estra-1,3,5(10)-trien-3-ol 431901-72-3P 431901-73-4P  
 431901-75-6P 431901-77-8P 431901-83-6P 431901-89-2P  
 431901-91-6P  
 RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)  
 (preparation of 2-methoxyestradiol derivs. as antiangiogenic agents)

IT 1818-12-8P 4953-96-2P 6298-51-7P 6301-87-7P 6599-97-9P  
 7291-57-8P 10332-20-4P 32162-96-2P 41259-43-2P 94440-60-5P  
 165619-07-8P 165881-61-8P 192062-02-5P 229486-18-4P  
 431901-68-7P 431901-69-8P 431901-70-1P  
 431901-71-2P 431901-74-5P 431901-76-7P  
 431901-78-9P 431901-82-5P 431901-84-7P 431901-86-9P  
 431901-87-0P 431901-88-1P 431901-92-7P 431901-93-8P 431901-94-9P  
 431901-95-0P 431901-96-1P 431901-97-2P 431901-98-3P  
 431901-99-4P 431902-00-0P 431902-01-1P 431902-02-2P 431902-03-3P  
 431902-04-4P 431902-05-5P 431902-06-6P 431902-07-7P 431902-08-8P  
 431902-09-9P  
 RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
 (preparation of 2-methoxyestradiol derivs. as antiangiogenic agents)

IT 53-16-7, Estrone, reactions 64-18-6, Formic acid, reactions 100-39-0,  
 Benzyl bromide 106-95-6, Allyl bromide, reactions 362-07-2,  
 2-Methoxyestradiol 1530-32-1, Ethyl triphenylphosphonium bromide  
 1779-49-3, Methyl triphenylphosphonium bromide 1779-51-7, Butyl  
 triphenylphosphonium bromide 4784-77-4, Crotyl bromide 5815-08-7,  
 tert-Butoxy bis(dimethylamino)methane 6228-47-3, Propyl  
 triphenylphosphonium bromide 17640-15-2, Methyl cyanoformate  
 RL: RCT (Reactant); RACT (Reactant or reagent)  
 (preparation of 2-methoxyestradiol derivs. as antiangiogenic agents)

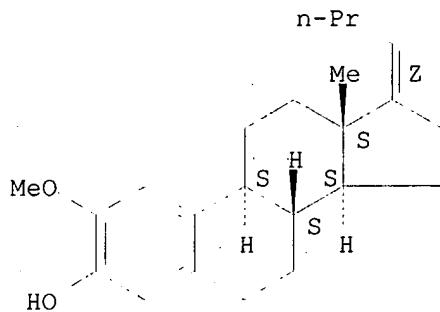
IT 26356-54-7P 26357-07-3P 93949-26-9P 431901-79-0P 431901-80-3P  
 431901-81-4P 431901-85-8P 431901-90-5P  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
 (preparation of 2-methoxyestradiol derivs. as antiangiogenic agents)

IT 431901-77-8P  
 RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)  
 (preparation of 2-methoxyestradiol derivs. as antiangiogenic agents)

RN 431901-77-8 HCAPLUS

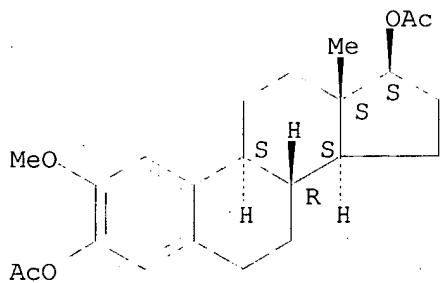
CN 19,21-Dinorchola-1,3,5(10),17(20)-tetraen-3-ol, 2-methoxy-, (17Z)- (9CI)  
 (CA INDEX NAME)

Absolute stereochemistry.  
Double bond geometry as shown.



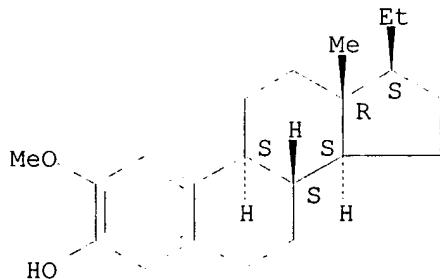
IT 7291-57-8P 229486-18-4P 431901-68-7P  
 431901-70-1P 431901-71-2P 431901-74-5P  
 431901-76-7P 431901-78-9P 431901-97-2P  
 RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU  
 (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES  
 (Uses)  
 (preparation of 2-methoxyestradiol derivs. as antiangiogenic agents)  
 RN 7291-57-8 HCPLUS  
 CN Estra-1,3,5(10)-triene-3,17-diol, 2-methoxy-, diacetate, (17 $\beta$ )- (9CI)  
 (CA INDEX NAME)

Absolute stereochemistry.



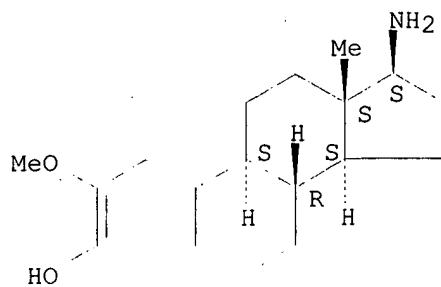
RN 229486-18-4 HCPLUS  
 CN 19-Norpregna-1,3,5(10)-trien-3-ol, 2-methoxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 431901-68-7 HCPLUS  
 CN Estra-1,3,5(10)-trien-3-ol, 17-amino-2-methoxy-, (17 $\beta$ )- (9CI) (CA  
 INDEX NAME)

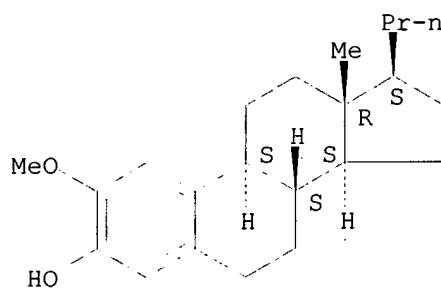
Absolute stereochemistry.



RN 431901-70-1 HCPLUS

CN Estra-1,3,5(10)-trien-3-ol, 2-methoxy-17-propyl-, (17 $\beta$ )- (9CI) (CA INDEX NAME)

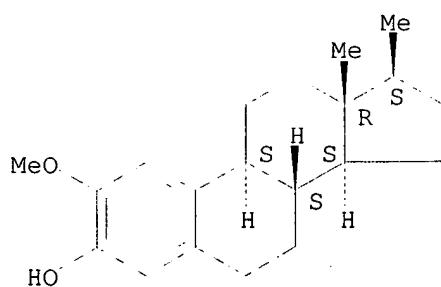
Absolute stereochemistry.



RN 431901-71-2 HCPLUS

CN Estra-1,3,5(10)-trien-3-ol, 2-methoxy-17-methyl-, (17 $\beta$ )- (9CI) (CA INDEX NAME)

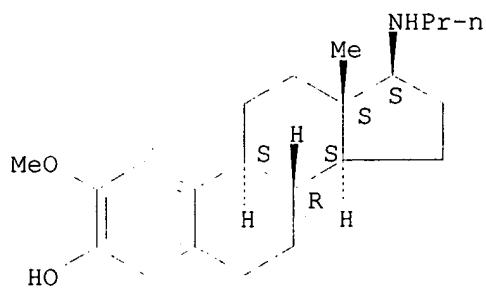
Absolute stereochemistry.



RN 431901-74-5 HCPLUS

CN Estra-1,3,5(10)-trien-3-ol, 2-methoxy-17-(propylamino)-, (17 $\beta$ )- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

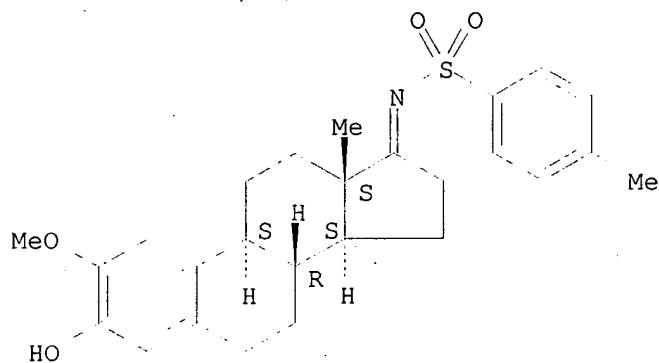


RN 431901-76-7 HCAPLUS

CN Benzenesulfonamide, N-(3-hydroxy-2-methoxyestra-1,3,5(10)-trien-17-ylidene)-4-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

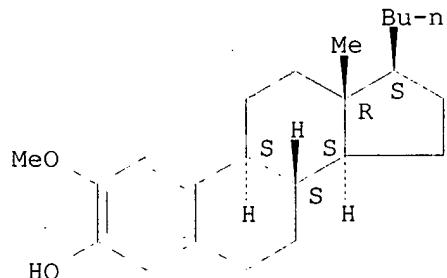
Double bond geometry unknown.



RN 431901-78-9 HCAPLUS

CN 19,21-Dinorchola-1,3,5(10)-trien-3-ol, 2-methoxy- (9CI) (CA INDEX NAME)

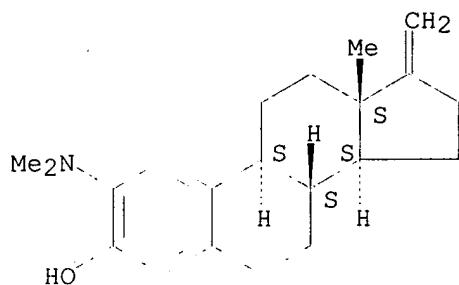
Absolute stereochemistry.



RN 431901-97-2 HCAPLUS

CN Estra-1,3,5(10)-trien-3-ol, 2-(dimethylamino)-17-methylene-, hydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.



● HCl

=> d his

(FILE 'HOME' ENTERED AT 09:07:56 ON 21 DEC 2003)  
DEL HIS

FILE 'REGISTRY' ENTERED AT 09:10:37 ON 21 DEC 2003

E C20H26O2/MF

SET COST OFF

L1 428 S E3 AND C5-C6-C6-C6/ES AND 4/NR  
L2 8 S L1 AND 17 METHYLENE  
L3 1 S L2 AND 2 METHOXY  
SEL RN  
L4 0 S E1/CRN

FILE 'HCAOLD' ENTERED AT 09:13:35 ON 21 DEC 2003

L5 0 S L3

FILE 'USPATFULL, USPAT2' ENTERED AT 09:13:39 ON 21 DEC 2003

L6 1 S L3

FILE 'HCAPLUS' ENTERED AT 09:13:41 ON 21 DEC 2003

L7 2 S L3

FILE 'REGISTRY' ENTERED AT 09:14:10 ON 21 DEC 2003

FILE 'USPATFULL, USPAT2' ENTERED AT 09:14:17 ON 21 DEC 2003

FILE 'HCAPLUS' ENTERED AT 09:14:30 ON 21 DEC 2003

FILE 'REGISTRY' ENTERED AT 09:15:35 ON 21 DEC 2003

E C5-C6-CC6-C6/ES

E C5-C6-C6-C6/ES

L8 243537 S E3  
L9 STR  
L10 50 S L9 CSS SAM SUB=L8  
L11 4643 S L9 CSS FUL SUB=L8  
SAV TEMP L11 QAZI939/A  
L12 STR L9  
L13 STR L9  
L14 50 S L13 CSS SAM SUB=L8  
L15 4643 S L13 CSS FUL SUB=L8  
SAV L15 QAZI939A/A  
L16 3 S L12 CSS SAM SUB=L15  
L17 50 S L12 CSS FUL SUB=L15

SAV L17 QAZI939B/A  
 L18 4593 S L15 NOT L17  
 L19 STR L12  
 DEL QAZI939/A  
 DEL QAZI939B/A  
 L20 STR L19  
 L21 50 S L20 CSS SAM SUB=L15  
 L22 1158 S L20 CSS FUL SUB=L15  
 SAV L22 QAZI939B/A  
 L23 3485 S L15 NOT L22  
 SAV L23 QAZI939C/A  
 L24 STR L20  
 L25 0 S L24 CSS SAM SUB=L15  
 L26 10 S L24 CSS FUL SUB=L15  
 SAV L26 QAZI939D/A  
 L27 9 S L26 NOT L3  
 L28 STR  
 L29 0 S L28 CSS SAM SUB=L15  
 L30 STR L28  
 L31 0 S L30 CSS SAM SUB=L15  
 L32 0 S L30 CSS FUL SUB=L15  
 SAV L32 QAZI939E/A  
 L33 STR L30  
 L34 0 S L33 CSS SAM SUB=L15  
 L35 0 S L33 CSS FULL SUB=L15  
 SAV L35 QAZI939F/A

FILE 'HCAOLD' ENTERED AT 09:46:24 ON 21 DEC 2003  
 L36 0 S L27

FILE 'USPATFULL, USPAT2' ENTERED AT 09:46:29 ON 21 DEC 2003  
 L37 5 S L27

FILE 'HCAPLUS' ENTERED AT 09:46:41 ON 21 DEC 2003  
 L38 9 S L27  
 L39 2 S L38 AND ENTREMED?/PA,CS  
 L40 3 S L38 AND (AGOSTON ? OR SHAH ? OR HUNSUCKER ? OR PRIBLUDA ? OR  
 L41 9 S L38-L40

FILE 'REGISTRY' ENTERED AT 09:48:58 ON 21 DEC 2003

FILE 'USPATFULL, USPAT2' ENTERED AT 09:49:31 ON 21 DEC 2003

FILE 'HCAPLUS' ENTERED AT 09:49:47 ON 21 DEC 2003  
 L42 2 S (US20020082433 OR US20020147183)/PN  
 L43 2 S (WO2001-US26490 OR US2001-933894# OR WO2001-US26128 OR US2001  
 L44 3 S L42, L43  
 L45 1 S L39, L40 NOT L44  
 L46 1 S US2002-361267#/AP, PRN  
 L47 4 S L44, L46  
 E AGOSTON G/AU  
 L48 24 S E5, E9, E10  
 E SHAH J/AU  
 L49 148 S E3, E9  
 E SHAH JAMSHEDE/AU  
 L50 29 S E3, E4, E5  
 E HUNSUCKER K/AU  
 L51 7 S E4, E5  
 E PRIBLUDA V/AU  
 L52 35 S E3-E8  
 E LAVALLEE T/AU  
 L53 16 S E4, E5  
 E LA VALLEE T/AU

L54            E GREEN S/AU  
 196 S E3,E15,E16  
 E GREEN SHAWN/AU  
 L55            60 S E3-E5  
 E HERBSTRITT C/AU  
 L56            7 S E4-E6  
 E ZHAN X/AU  
 L57            31 S E3,E8  
 E ZHAN XIA/AU  
 L58            6 S E38,E39  
 E TRESTON A/AU  
 L59            54 S E3-E8  
 E ENTREMED/PA,CS  
 L60            79 S E3-E15

FILE 'REGISTRY' ENTERED AT 09:56:32 ON 21 DEC 2003  
 L61            4633 S L15 NOT L3,L26

FILE 'HCAPLUS' ENTERED AT 09:59:04 ON 21 DEC 2003  
 L62            63865 S L61  
 L63            4 S L62 AND L47  
 L64            18 S L62 AND L48-L60  
 L65            14 S L64 NOT L63  
 SEL HIT RN L63  
 SEL HIT RN L65

FILE 'REGISTRY' ENTERED AT 10:00:20 ON 21 DEC 2003  
 L66            54 S E1-E54  
 L67            11 S E55-E65  
 L68            50 S L66 NOT L67  
 L69            11 S L68 AND (C23H32O2 OR C23H24O2 OR C22H33NO2 OR C19H27NO2 OR C2  
 L70            9 S L69 NOT C20H28O2  
 L71            2 S L69 NOT L70  
 L72            1 S L71 NOT 165881-61-8  
 L73            10 S L70,L72  
 L74            40 S L68 NOT L73  
 L75            2 S L74 AND (C23H34O2 OR C26H32N2O4S)  
 L76            12 S L73,L75

FILE 'HCAOLD' ENTERED AT 10:10:31 ON 21 DEC 2003  
 L77            4 S L76

FILE 'HCAPLUS' ENTERED AT 10:10:45 ON 21 DEC 2003  
 L78            30 S L76  
 L79            27 S L78 AND (PD<=20010208 OR PRD<=20010208 OR AD<=20010208)  
 L80            3 S L78 AND L47-L60  
 L81            29 S L63,L79-L80  
 L82            2 S L78 NOT L81

FILE 'HCAOLD' ENTERED AT 10:12:46 ON 21 DEC 2003  
 SEL AN L77  
 EDIT /AN /OREF

FILE 'HCAPLUS' ENTERED AT 10:13:12 ON 21 DEC 2003  
 L83            6 S E66-E69  
 L84            5 S L83 NOT MAZUR ?/AU  
 L85            31 S L81,L84  
 L86            26 S L81 NOT L84

FILE 'REGISTRY' ENTERED AT 10:14:28 ON 21 DEC 2003

FILE 'HCAOLD' ENTERED AT 10:14:44 ON 21 DEC 2003

qazi - 09 / 939208

Page 141

FILE 'HCAPLUS' ENTERED AT 10:14:51 ON 21 DEC 2003

L87           3 S L84 AND L78  
L88           5 S L84,L87  
L89           22 S L86 NOT L63

=>

305812-81-1P 305812-83-3P 305812-85-5P 305812-87-7P 305812-89-9P  
 305812-91-3P 305812-93-5P 305812-95-7P 305812-97-9P 305812-99-1P  
 305813-01-8P 305813-03-0P 305813-05-2P 305813-07-4P 305813-09-6P  
 305813-10-9P 305813-12-1P 305813-14-3P 305813-15-4P 305813-16-5P  
 305813-17-6P 305813-19-8P 305813-20-1P 305813-21-2P 305813-22-3P  
 305813-23-4P 305813-25-6P 305813-26-7P 305813-27-8P 305813-28-9P  
 305813-30-3P 305813-32-5P 305813-34-7P 305813-36-9P 305813-38-1P  
 305813-39-2P 305813-40-5P 305813-41-6P 305813-42-7P 305813-43-8P  
 305813-44-9P 305813-45-0P 305813-46-1P 305813-47-2P 305813-48-3P  
 305813-49-4P 305813-50-7P 305813-51-8P 305813-52-9P 305813-53-0P  
 305813-54-1P 305813-55-2P 305813-56-3P 305813-57-4P 305813-58-5P  
 305813-59-6P 305813-60-9P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(synthesis of cholestane compds. with a c17-alkyl side chain and an aromatic A-ring for use in cell modulating therapy)

RE.CNT 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

- (1) Escaleira; 1993, 7, HCPLUS
- (2) Escaleira; J STEROID BIOCHEM MOL BIOL 1993, V45(4), P257 HCPLUS
- (3) Laing, S; US 3717627 A 1973
- (4) Lajeunesse; 1994, 23, HCPLUS
- (5) Lajeunesse; BONE MINER 1994, V24(1), P1 HCPLUS
- (6) Liel; 1992, 25, HCPLUS
- (7) Liel; ENDOCRINOLOGY (BALTIMORE) 1992, V130(5), P2597 HCPLUS
- (8) Mountford; 1999, 8, HCPLUS
- (9) Mountford; EXP HEMATOL (N Y) 1999, V27(3), P451 HCPLUS
- (10) Ruggieri, P; US 3562260 A 1971 HCPLUS

IT 229486-17-3P

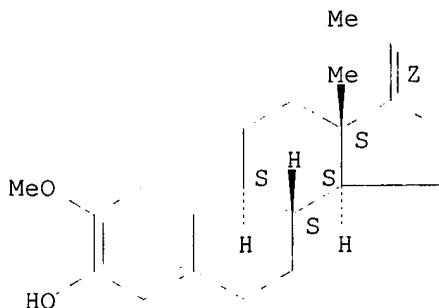
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(synthesis of cholestane compds. with a c17-alkyl side chain and an aromatic A-ring for use in cell modulating therapy)

RN 229486-17-3 HCPLUS

CN 19-Norpregna-1,3,5(10),17(20)-tetraen-3-ol, 2-methoxy-, (17Z)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.  
Double bond geometry as shown.



L41 ANSWER 8 OF 9 HCPLUS COPYRIGHT 2003 ACS on STN

AN 1999:460438 HCPLUS

DN 131:88083

ED Entered STN: 28 Jul 1999

TI Preparation of estrone sulfamate inhibitors of estrone sulfatase

IN Tanabe, Masato; Peters, Richard H.; Chao, Wan-Ru; Shigeno, Kazuhiko

PA SRI International, USA

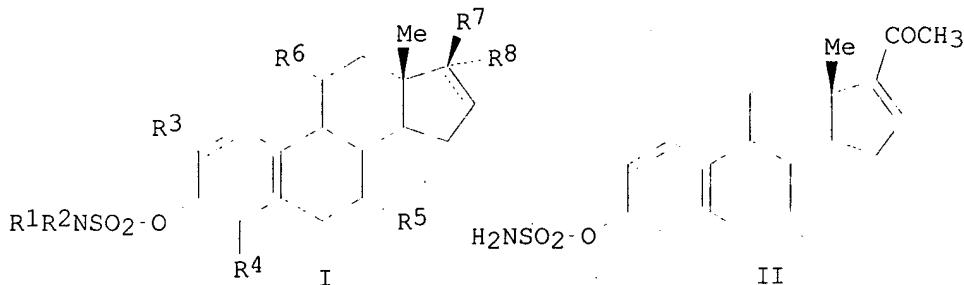
SO PCT Int. Appl., 102 pp.

CODEN: PIXXD2

DT Patent  
 LA English  
 IC ICM C07J041-00  
 ICS A61K031-565; A61K031-57; A61K031-575  
 CC 32-3 (Steroids)  
 Section cross-reference(s): 2, 63

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9933858	A2	19990708	WO 1998-US27333	19981221
	W: AU, CA, JP, KR RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	US 6046186	A	20000404	US 1997-997416	19971224
	CA 2318349	AA	19990708	CA 1998-2318349	19981221
	AU 9919416	A1	19990719	AU 1999-19416	19981221
	AU 751732	B2	20020829		
	EP 1042354	A2	20001011	EP 1998-964243	19981221
	R: DE, FR, GB, IT, NL JP 2001527089	T2	20011225	JP 2000-526534	19981221
PRAI	US 1997-997416	A	19971224		
	WO 1998-US27333	W	19981221		
OS	MARPAT 131:88083				
GI					



AB Novel compds. of formula I [R<sub>1</sub>, R<sub>2</sub> = H, alkyl, etc.; R<sub>3</sub> = H, CN, NO<sub>2</sub>, COOH, alkoxy carbonyl, etc.; R<sub>4</sub> = H, NO<sub>2</sub>, (substituted) amino; R<sub>5</sub>, R<sub>6</sub> = H, alkyl; R<sub>7</sub>, R<sub>8</sub> = H, alkyl, alkenyl, alkynyl, alkoxy, acyl, acyloxy, etc.; R<sub>7</sub>, R<sub>8</sub> = oxo, alkylidene, etc.] are prepared as inhibitors of estrone sulfatase. Thus, II is prepared from ethynodiol in 4 steps. and showed estrone sulfatase inhibitory activity of IC<sub>50</sub> = 21 pM. Pharmaceutical compns. and methods for using I to treat estrogen-dependent disorders are provided.

ST estrone sulfamate prep'n estrone sulfatase inhibitor

IT Estrogens

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
 (antiestrogens; preparation of estrone sulfamates as inhibitors of estrone sulfatase)

IT Antitumor agents

(preparation of estrone sulfamates as inhibitors of estrone sulfatase)

IT 59298-96-3, Estrone sulfatase

RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)  
 (inhibitors; preparation of estrone sulfamates as inhibitors of estrone sulfatase)

IT 185910-34-3P 185910-42-3P 208924-86-1P 208924-87-2P 229485-78-3P

229485-79-4P 229485-80-7P 229485-81-8P 229485-82-9P 229485-83-0P  
 229485-84-1P 229485-85-2P 229485-86-3P 229485-87-4P 229485-88-5P  
 229485-89-6P 229485-90-9P 229485-91-0P 229485-92-1P 229485-93-2P  
 229485-94-3P 229485-95-4P 229485-96-5P 229485-97-6P 229485-98-7P  
 229485-99-8P 229486-00-4P 229486-01-5P 229486-02-6P 229486-03-7P  
 229486-04-8P 229486-05-9P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of estrone sulfamates as inhibitors of estrone sulfatase)

IT 50-28-2, Estradiol, reactions 53-16-7, Estrone, reactions 57-63-6,  
 Ethynodiol 108-01-0, N,N-Dimethylethanamine 109-77-3,  
 Malononitrile 362-08-3 867-13-0, Triethylphosphonoacetate 1779-51-7,  
 Butyltriphenylphosphonium bromide 4584-46-7 5407-04-5 6228-47-3,  
 Propyltriphenylphosphonium bromide 7678-95-7 67530-18-1 229486-27-5  
 RL: RCT (Reactant); RACT (Reactant or reagent)

(preparation of estrone sulfamates as inhibitors of estrone sulfatase)

IT 858-98-0P 1667-98-7P 4736-62-3P 5774-17-4P 5779-47-5P 5976-73-8P  
 5976-74-9P 6599-97-9P 13879-55-5P 13879-57-7P 14030-45-6P  
 14846-63-0P 14982-15-1P 15001-40-8P 22787-09-3P 23880-59-3P  
 31559-52-1P 57711-40-7P 59077-04-2P, 19-Norpregna-1,3,5(10)-trien-3-ol  
 59452-15-2P 59452-16-3P, 19,21-Dinorchola-1,3,5(10)-trien-3-ol  
 64215-82-3P 67519-62-4P 71716-18-2P 96111-26-1P 101766-63-6P  
 115208-23-6P 115387-92-3P 116627-15-7P 116627-20-4P 120574-27-8P  
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 229486-24-2P 229486-25-3P 229486-26-4P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of estrone sulfamates as inhibitors of estrone sulfatase)

IT 229486-17-3P

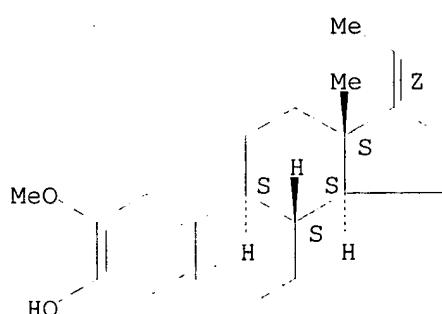
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of estrone sulfamates as inhibitors of estrone sulfatase)

RN 229486-17-3 HCPLUS

CN 19-Norpregna-1,3,5(10),17(20)-tetraen-3-ol, 2-methoxy-, (17Z)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.  
 Double bond geometry as shown.



TI Preparation of steroid inhibitors of estrone sulfatase and associated pharmaceutical compositions and methods of use

IN Tanabe, Masato; Peters, Richard H.; Chao, Wan-ru; Shigeno, Kazuhiko

PA SRI International, USA

SO U.S., 23 pp.

CODEN: USXXAM

DT Patent

LA English

IC ICM A61K031-58

ICS C07J071-00

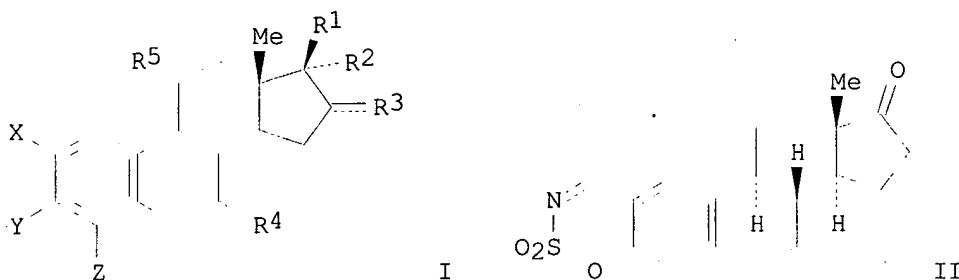
NCL 514176000

CC 32-3 (Steroids)

Section cross-reference(s): 1, 2

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 5763432	A	19980609	US 1997-794229	19970129
	US 5861388	A	19990119	US 1997-1601	19971231
	WO 9832763	A1	19980730	WO 1998-US1846	19980129
W: CA, JP, KR RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE					
PRAI	US 1997-794229		19970129		
OS	MARPAT 129:54482				
GI					



AB Estratriene derivs. of formula I [X and Y, or Y and Z, form an oxathiazine dioxide ring or a dihydro-oxathiazine dioxide ring; R1, R2 = H, alkyl, alkynyl, (substituted) OH; R1R2 = O, S, (substituted) CH2; R3 = H, halo, alkyl, CH2; R4 = H, alkyl; R5 = H, OH, alkyl, alkenyl, alkoxy, aryl, CH2] are prepared as inhibitors of estrone sulfatase. Pharmaceutical comps. and methods for using I to treat estrogen-dependent disorders are provided as well. Thus, estradiol is transformed into II in 3 steps. In an estrone sulfatase inhibition assay, II showed 5% inhibition at 9.3 nM.

ST estratriene deriv prepn estrone sulfatase inhibitor

IT 208758-20-7P 208758-22-9P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)  
(preparation of steroid inhibitors of estrone sulfatase)

IT 208758-16-1P 208758-17-2P 208758-21-8P 208758-23-0P 208758-25-2P

208758-33-2P 208758-34-3P 208758-35-4P 208758-36-5P 208758-37-6P

208758-38-7P 208758-39-8P 208758-41-2P 208758-43-4P 208758-48-9P

208758-52-5P 208758-54-7P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
(preparation of steroid inhibitors of estrone sulfatase)

IT 59298-96-3, Estrone sulfatase

RL: BPR (Biological process); BSU (Biological study, unclassified); MSC (Miscellaneous); BIOL (Biological study); PROC (Process)  
 (preparation of steroid inhibitors of estrone sulfatase)

IT 50-28-2, Estradiol, reactions 53-16-7, Estrone, reactions 57-63-6,  
 17 $\alpha$ -Ethynelestradiol 1530-32-1, Ethyltriphenylphosphonium bromide  
 1779-51-7, Butyltriphenylphosphonium bromide 4954-12-5 6228-47-3,  
 Propyltriphenylphosphonium bromide 7678-95-7 59077-04-2,  
 19-Norpregna-1,3,5(10)-trien-3-ol

RL: RCT (Reactant); RACT (Reactant or reagent)

(preparation of steroid inhibitors of estrone sulfatase)

IT 4736-62-3P 6599-97-9P 13879-55-5P 13879-56-6P 31559-62-3P  
 34111-53-0P 57711-40-7P 64215-82-3P 99898-93-8P 120574-27-8P  
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 208758-19-4P 208758-24-1P 208758-26-3P 208758-27-4P  
**208758-28-5P** 208758-29-6P 208758-30-9P 208758-31-0P  
 208758-32-1P 208758-40-1P 208758-42-3P 208758-44-5P 208758-45-6P  
 208758-46-7P **208758-47-8P** 208758-50-3P 208758-51-4P  
 208758-53-6P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT  
 (Reactant or reagent)

(preparation of steroid inhibitors of estrone sulfatase)

IT 208758-49-0P

RL: SPN (Synthetic preparation); PREP (Preparation)

(preparation of steroid inhibitors of estrone sulfatase)

RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

- (1) Babcock; US 4297350 1981 HCPLUS
- (2) Kuehne; US 3033860 1962 HCPLUS

IT 208758-26-3P 208758-27-4P 208758-28-5P  
**208758-47-8P**

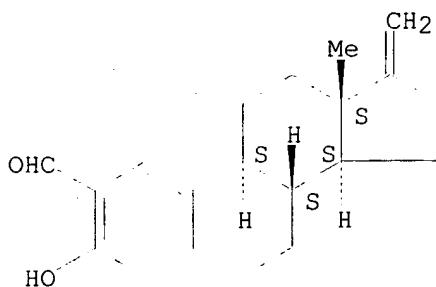
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT  
 (Reactant or reagent)

(preparation of steroid inhibitors of estrone sulfatase)

RN 208758-26-3 HCPLUS

CN Estra-1,3,5(10)-triene-2-carboxaldehyde, 3-hydroxy-17-methylene- (9CI)  
 (CA INDEX NAME)

Absolute stereochemistry.

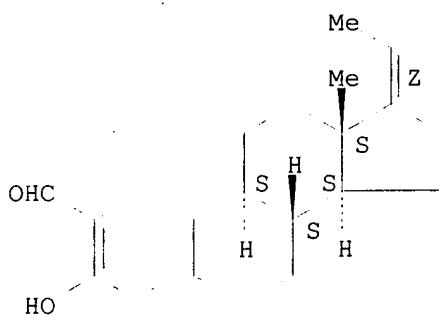


RN 208758-27-4 HCPLUS

CN 19-Norpregna-1,3,5(10),17(20)-tetraene-2-carboxaldehyde, 3-hydroxy-,  
 (17Z)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.

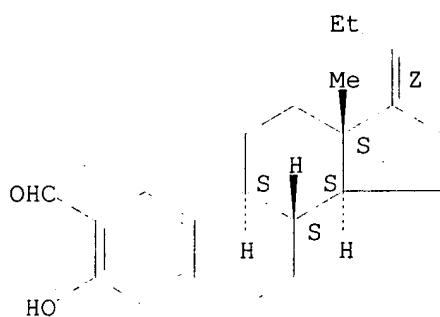


RN 208758-28-5 HCPLUS

CN Estra-1,3,5(10)-triene-2-carboxaldehyde, 3-hydroxy-17-propylidene-, (17Z)-  
(9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.

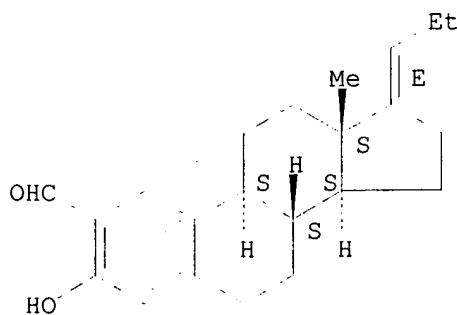


RN 208758-47-8 HCPLUS

CN Estra-1,3,5(10)-triene-2-carboxaldehyde, 3-hydroxy-17-propylidene-, (17E)-  
(9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.



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